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Issue 27

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Reader Feedback Form

To our readers: We are working in a large number of highly technical, specialized areas for which adequate Russian-English glossaries have yet to be compiled. We ask your help in improving the accuracy and specificity of our English terminology. Please fill out the form below whenever you encounter an incomprehensible, incongruous, awkward or otherwise inappropriate term. While we solicit all suggestions for improved renderings, the statement that a term is inappropriate provides us with useful information, even when no better alternative can be suggested. A copy of this form will appear in all future issues of the Digest. Thank you for your help.

Abstract Number	Incorrect or inappropriate term	Suggested rendering

PLEASE RETURN TO: Dr. Lydia Stone
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FROM THE EDITORS

This is Issue 27 of the USSR Space Life Sciences Digest. Articles presenting or discussing space flight data in this issue are: Biorhythms P1204, Botany P1213, Cardiovascular and Respiratory Systems P1202, Endocrinology P1203, and Musculoskeletal System P1222 and 1224. The coming issue of the Digest will be double, i.e., provide abstracts for two issues of the Soviet *Space Biology and Aerospace Medicine* journal. This issue will also mark the beginning of our use of an "expert panel" to provide technical editing of the digest. We expect that inclusion of his panel will improve the accuracy and appropriateness of the technical terminology used in the Digest. We would like to thank Drs. Gary Coulter and and F. Ronald Dutcher for acting as expert consultants for the current issue.

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MONOGRAPH:

M160(27/90) Vinogradov VV.

Gormony, Adaptatsiya i Sistemnyye Reaktsii Organizma; Гормоны, Адаптация и Системные Реакции Организма; [*Hormones, Adaptation, and Systemic Reactions.*]

Minsk: Nauka i Tekhnika; 1989.

[223 pages; 19 Tables; 56 Figures; 538 references]

Affiliation (book): Institute of Biochemistry; Belorussian Academy of Sciences

KEY WORDS: Adaptation; Endocrinology, Hormones, Stress; Biological Rhythms, Seasonal Rhythms; Metabolism; Cardiovascular and Respiratory System

Annotation: With reference to a wide range of experimental and clinical materials, the author analyzes the role played by hormones in supporting rhythmic homeostatic functions responsible for adaptation at the cellular level and for the development of systemic reactions to stress. Hormonal mechanisms underlying seasonal rhythms in metabolic functions are discussed. A rationale is presented for using biochemical indicators of the stress response in medical practice for diagnosing latent forms of circulatory insufficiency in cardiovascular pathology. Biochemical, physiological, and medical aspects of adaptation, its appropriateness and failures are discussed. This monograph is intended for biochemists, physiologists, and medical personnel.

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PAPER:

P1230(27/90) Mel'nik SG, Shakula AV, Gladkikh FD.

The effect of workload on the functional state of flight crews of ship-based aviation.

Voyenno-Meditsinskiy Zhurnal.

1989(7): 54-57.

[No references]

Authors' Affiliations: USSR Medical Corps

Aviation Medicine, Functional State, Cardiovascular and Respiratory Systems
Humans, Air Crews, Ship-Based Aviation
Human Performance, Workload

Abstract: Traditional physiological methods were used to study the functions of the cardiovascular and respiratory systems and reserve capacities of 26 helicopter pilots and navigators in ship-based aviation before and after flights performed in the course of long-duration cruises. At low latitudes, mean data suggest a hypotonic reaction to flight conditions, attributed by the authors to heat and long periods of relative hypokinesia. After 2- and 3-hour flights, only systolic pressure decreased for pilots, while both diastolic and systemic pressure decreased in navigators. Results were of similar magnitude for both durations of flight. Recovery of blood pressure was not complete after 58 hours. Heart rate remained the same postflight for pilots but increased in navigators. After 2- and 3-hour flights at low latitudes, respiration rate increased significantly and reserve capacity (measured by performance on breath holding tests) decreased. When flight duration increased from 2 to 3 hours, respiration rate increased still further and reserve capacity decreased. Fifty-eight hours after the 2-hour flight, most respiratory parameters had recovered, but this was not the case for the 3-hour flight.

In an additional study, the same group of six helicopter pilots performed analogous flight missions at high and low latitudes. Cardiovascular response was adequate at high latitudes, with moderate increase in systolic and diastolic pressure, and increased heart rate, normalizing after 16 hours. At low latitudes, blood pressure decreased and heart rate increased significantly, and these changes persisted for more than 16 hours, normalizing completely only 58 hours postflight. After flight at high latitudes, breathing rate increased only insignificantly and reserve capacities decreased moderately, with normalization occurring after 16 hours. Analogous flights at low latitudes led to greater increases in respiration rate and significant decreases in respiratory reserve.

Results of a questionnaire revealed that pilots and navigators considered the optimal flight workload to be 3 ± 1 hours per shift, 6 ± 1 hours per week, 17 ± 1 hour per month, and 104 ± 3 hours per year.

Table 1: Dynamics of cardiovascular parameters in helicopter crews flying at high latitudes

Table 2: Dynamics of cardiovascular parameters in helicopter crews flying at low latitudes

Figure 1: Change in parameters of functional state of the cardiovascular system of pilots flying at high latitudes

Figure 2: Change in parameters of functional state of the cardiovascular system of pilots flying at low latitudes

AVIATION MEDICINE

Figure 3: Change in parameters of functional state of the respiratory system of pilots flying at high latitudes

Figure 4: Change in parameters of functional state of the respiratory system of pilots flying at low latitudes

BOOK REVIEW:

BR17(27/90)*Gyurdzhian AA.

Review of: Ernsting J, and King, et al. (Editors).

Aviation Medicine.

London: Butterworth 1988, 738 pages.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 92-94; 1989.

NOTE: Although this is a translation of review of a British, not a Soviet book. It may be of some interest to our readers to find out what English-language works Soviet scientists are aware of and how such literature is reviewed.

KEY WORDS: Aviation Medicine, Human Performance, Aviation Psychology, Biodynamics, Thermal Stress; Biological Rhythms

The second edition of the British handbook on aviation medicine is intended for physicians undergoing postgraduate specialization training in aviation medicine.

Both the scientific editors and the majority of authors (42 of whom participated in preparing the handbook) - are members of the Medical Corps of the British Royal Air Force, mainly at the Institute of Aviation Medicine in Farnborough. Although the authors are all British, the work commendably considers ideas and scientific data of researchers from other nations and also the official regulations of the International Organization of Civil Aviation.

The current edition has been revised to such a great extent that it is not strictly accurate to call it the second edition of the handbook published in 1978 (Aviation Medicine, Editor, G. Dhenin [sic], London, Tri-Med Books Ltd. 1978). Only 25% of the authors contributing to the second edition had contributed to the first. Even the few chapters written by the same authors have undergone fairly major revisions in light of the latest advances in aviation medicine. It is an added convenience that the second edition has been published as a single volume, while the first was in two volumes.

The handbook comprises 10 parts, 55 chapters and 2 appendices. The first five parts are devoted to issues in aviation physiology, and the last five to clinical problems, working conditions and hygiene in aviation, and also aviation pathology and investigation of aircraft accidents.

Reflecting the development of aviation during the last 10 years (after publication of the first volume), the main focus in aviation medicine has shifted from study of the effects of flight factors and conditions on autonomic and somatic functions (respiration, cardiovascular functioning, biodynamics, thermal regulation) to research on psychophysiological status and job performance, particularly in flight crews. For this reason, the greatest differences between the first and second editions can be found in sections dealing with these topics. For example, Part 5 "Aviation Psychology," has been rewritten completely, while the chapters in Part 9 devoted to the clinical aspects of aviation medicine have been substantially reworked and expanded. Part 10, which discusses methods for investigating aircraft accidents and results in aviation pathology is completely new.

Let us turn to analysis of the contents of the handbook. In Part 1 ("Environmental Pressure") data concerning the Earth's atmosphere, air pressure differentials, the principles of respiratory physiology, hypoxia and hyperventilation, oxygen equipment, full pressure suits, pressurized cabins and partial pressure suits, as well as the effects of toxic gases and vapors are discussed thoroughly and clearly.

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Part 2 ("Biodynamics") relatively briefly (compared to two other modern handbooks), but in sufficient depth, considers the effects of prolonged acceleration of various types and of vibration, as well as measures taken to protect flight crews against their effects. This section describes the dynamics and mechanisms of forces acting on humans in aircraft accidents and the associated injuries (particularly head injuries) in flight crews and passengers, means of protection against these forces, and methods for escaping from aircraft.

Part 3 ("Thermal Stress and Survival") is devoted to heat exchange and thermal regulation in humans, ways to protect flight crews from thermal stress, and survival techniques in adverse thermal and climatic conditions, particularly after accidents. The Institute of Aviation Medicine traditionally sponsors a major research program on thermal regulation and temperature stress in special laboratories in which important and well-designed work is conducted.

Part 4 ("Sense Organs") devoted to issues related to the sense organs is unique. In three chapters one of the most famous specialists in this area, A.J. Benson, considers in detail the problems of spatial orientation in pilots and also the critical problem of motion sickness. In addition, this part contains chapters devoted to current data on pilot vision and the interrelated issues of noise and communication (radiocommunications) under flight conditions.

Part 5 ("Aviation Psychology") is very impressive. It cites the psychological results most relevant to the performance of flight crews. It considers the processes of attention, particularly allocation of pilot attention, cognition, decision-making and memory (e.g., memory for an immediately preceding flight accident). Part 5 provides a good presentation of the problems of stress and approaches to evaluating the workload of a flight crew, problems of individual psychophysiological differences, personality traits, selection of personnel and various training methods. Significant emphasis is placed on ergonomics, particularly the ergonomic characteristics of new display and control systems. For the first time in any handbook of aviation medicine there is a chapter devoted to the social psychology of aircraft crews.

Finally, several chapters in part 5 provide glossaries of relevant terms. This is very important since technical psychological terminology is not always known by aviation physicians.

Part 6 ("Special Types of Flight") contains very useful information about the medical aspects of various types of flights of civil and military aircraft.

Chapters 7 and 8 ("Commercial Aviation and Health," and "Health and Hygiene") consider problems of public health relevant to civil aviation. International regulations for maintaining the health of aircraft crews and passengers, and rules for transporting the sick and handicapped are cited, along with the medical standards for flight certification examinations. Problems related to maintaining health, the hygiene of aircraft flights and airports, quarantine, and immunological and epidemiological aspects of international flights, regulations concerning transport of animals, and disinfection and extermination of rats and insects are discussed. The chapter discussing maintenance of the health of ground personnel, particularly technical aviation personnel, whose working conditions are sometimes very adverse, is very timely.

Part 9 ("Clinical Aspects of Aviation Medicine") will be especially interesting for Soviet specialists. In Soviet handbooks and proceedings of meetings on aviation medicine, clinical issues are emphasized much less than in analogous foreign works. This contributes to some degree of isolation of aviation physicians from the rest of medicine and does not assist their theoretical and clinical training as doctors and specialists in flight certification examinations.

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Two chapters in Part 9 are devoted to diurnal biological rhythms, work/rest schedules, sleep and wakefulness, job performance and appropriate medical recommendations. Next there are nine chapters devoted to purely clinical aspects of aviation medicine: diseases of the cardiovascular, respiratory, and digestive systems; kidney disease; diabetes; obesity; thyrotoxicosis; anemia; sickle cell anemia; tumors; psychiatric; neurological; otorhinolaryngological; ophthalmological and orthopedic problems; alcoholism; drug dependence; and sexual dysfunction.

It should be noted that all the clinical issues are discussed as they pertain to occupational diseases of aviation personnel and to health risk conditions and factors relevant to job performance, and the requirements for flight certification examinations. Thus, for example, the chapter devoted to otorhinolaryngology elucidates issues relevant to the harmful effects of noise; the chapter on ophthalmology focuses on vision requirements for flight crews; the chapter on orthopedics considers typical skeletal injuries (particularly to the spine) in aircraft accidents and ejection, etc. These discussions consider modern advances in medical science and new regulations for flight certification examinations, including those of the ICAO. The section devoted to medical ethics in the work of the medical corps for civil and military aviation is interesting.

The final chapter, Chapter 10, ("Investigation of Aircraft Accidents") is new and extremely useful. It elucidates the administrative and legal issues involved in such investigations, taking account of ICAO requirements and the set of methods used by specialists in aviation pathology, including the methods for identifying plane crash victims by their teeth and dental work.

The first appendix contains seven tables of units of measurement with the appropriate symbols, abbreviations, and coefficients for transforming units from one system to another. The second appendix contains a 14-page detailed subject index.

An important advantage of this book is its success in combining accurate and simple forms of presentation with a high concentration of information and modern factual material in the relevant areas of aviation medicine. At the end of each chapter is a list of cited sources in the literature to enable deeper study.

The authors' texts are adequately illustrated with graphs, diagrams, figures, and photographs. All this makes the book under review valuable both as a handbook and a reference work. In completeness and breadth of coverage the book resembles the handbook on aviation physiology ("A Textbook of Aviation Physiology" edited by J.A. Gilles, et al., Oxford, Pergamon Press, 1965, 1226 pages) published in England.

The book undoubtedly will be of interest of Soviet aviation and space physicians, and also to those working in related disciplines.

BIOLOGICAL RHYTHMS

PAPER:

P1204(27/90)* Alpatov Am, Yevstratov YuA., Chernyshev VB, Lebedev MI, Zotov VA.
Free running circadian rhythms in the darkling beetle after space flight.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(6): 31-33; 1989.
[9 references; 5 in English]

Biological Rhythms, Circadian Rhythms, Free-Running, Motor Activity
Beetles, Darkling
Space Flight, COSMOS-1887

Abstract: Darkling beetles (*Trigonoscelis gigas*), which are capable of maintaining free-running rhythms of motor activity for long periods under conditions of constant darkness, were selected as subjects in this experiment on the effects of space flight on biological rhythms. Two months preflight, the beetles were caught and maintained in a cage with a 16:8 light to darkness ratio. During the experiment each beetle was housed in an individual cell where motor activity was recorded. Throughout the experimental period, the insects were maintained in total darkness. Motor activity was recorded for 8 days preflight and 10 days postflight and during the 14-day flight on COSMOS-1887. After the flight the animals were returned to the cage and their circadian rhythms resynchronized. A 24-hour control experiment was run on the ground during which the insects were exposed to vibration such as occurs during spacecraft take-off and landing, and also chilling at 15° such as occurred immediately after landing.

In space, six of the seven beetles displayed a reliable decrease in the period of their circadian rhythm of motor activity. In two of these, the period gradually recovered to normal in 5-7 days after landing. Vibration did not affect the rhythm, and chilling completely depressed the beetles' activity but did not affect subsequent parameters. In one insect chilling did displace the rhythm by 3 hours. No changes in period occurred in the control experiment.

The effect observed here — decrease in the spontaneous period of the circadian rhythm under conditions of weightlessness — is important because period duration is a fundamental characteristic of the circadian system and is known to be little affected by external factors, with the exception of those that act as time cues (light or, less frequently, temperature). Gravity is not a time cue, which makes the observed effect somewhat surprising. However, it has been found previously that period of circadian rhythms may be increased by prolonged exposure to centrifugation (in primates). In both cases the effect, while statistically significant, did not exceed the bounds of the norm. This result suggests that in space the biologically optimum duration of a "day" may differ from that on Earth.

Table: Duration of the period (τ , hr) of free-running circadian rhythms of motor activity in insects

Beetle #	Preflight	Postflight	p (t-test)
1	25.0±0.4	23.7±0.2	<0.025
2	24.3±0.2	21.6±0.5*	<0.0005
3	23.7±0.2	24.3±0.4	n.s.
4	23.8±0.4	22.0±0.7*	<0.05
5	23.7±0.2	22.4±0.4	<0.01
6	24.1±0.3	23.7±0.2	n.s.
7	24.3±0.2	22.9±0.4	<0.005

BIOLOGICAL RHYTHMS

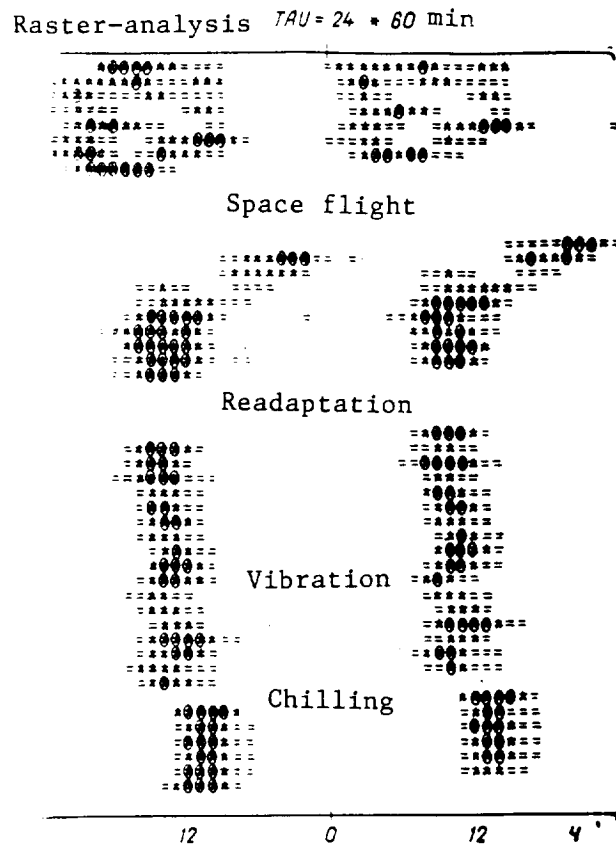


Figure: Free-running circadian rhythm of motor activity of beetle number 2
 From the top: Day of experiment. darkness of each character corresponds to the total number of movements in an hour.

MONOGRAPH:

M161(27/9) Khantseverov FR, Ostroukhov VV.

Modelirovaniye Kosmicheskikh Sistem Izucheniya Prirodnkh Resursov Zemli; Моделирование Космических Систем Изучения Природных Ресурсов Земли; [*Modeling of Space Systems for Studying the Earth's Natural Resources*]

Moscow: Mashinostroyeniye; 1989.

[264 pages; 69 Figures]

KEY WORDS: Biospherics, Mathematical Modeling, Space Systems, Remote Sensing, Natural Resources

Annotation: This book considers theoretical and practical aspects of modeling space systems for studying the Earth's natural resource, citing an original set of multifactor models of different physical types, with varying capacity and structural complexity. The book is intended for engineers in the area of cosmonautics, and also for specialists working on issues of systems analysis and the mathematical and physical modeling of space systems of scientific and economic significance.

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PAPER:

P1213(27/90)* Nevzgodina LV, Maksimova YeN, Kaminskaya YeV.

The effects of single hits by heavy ions of galactic cosmic radiation on *Lactuca sativa* seeds flown on board Salyut-6 and Salyut-7 space stations.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 66-70; 1989.

[15 references; 6 in English]

Genetics, Aberrations

Botany, Lettuce, Seeds

Space Flight, Long-term, Salyut-6, Salyut-7; Radiobiology, Heavy Ions

Abstract: Air-dried seeds of lettuce, *Lactuca sativa* were exposed on board Salyut-6 for 123 days and on board Salyut-7 for periods of 40, 201, and 457 days. All of the biostacks used in these experiments were located in the inhabited portion of the spacecraft and were maintained under controlled conditions. Each biostack consisted of layers of seeds placed in "monolayers" alternating with physical detectors that recorded the paths of cosmic heavy ions. Nitracellulose detectors recorded heavy ions with charge of $Z \geq 6$ and $LET \geq 200 \text{ keV}/\mu\text{m}$. After the samples were returned to Earth, the biostacks were disassembled. To identify heavy ion tracks the detectors were soaked in an alkaline solution and then were examined in a stack which had the same coordinate system as the ones returned from space. Joint examination of the biological layer and detectors made it possible to identify the seeds through which heavy ions had passed. Flux density and fluence of heavy ions were measured. Dosimetry was performed using thermoluminescent detectors. Integral absorbed doses were measured. Two weeks after the return to Earth, seeds in all conditions were moistened with tap water and germinated in Petri dishes. One day after hydration and subsequently during growth, cells were fixed in a 1:3 mixture of acetic acid and alcohol and a cytogenetic analysis was performed during the first mitosis. Seed viability (day 3) and germination (day 7) were noted. Radiation effects were assessed by the presence of various chromosomal restructurings observed during anaphase and telophase. The following groups were utilized: flight seeds hit and not hit by heavy particles, and ground control seeds.

Dosimetry measurements showed an increase in fluence and dose as flight duration increased from 40 to 457 days.

Germination of the flight seeds was somewhat delayed, especially those seeds hit by heavy ions. Delays were noted for all durations of flight. Viability was depressed in flight seeds on day 3 after moistening; however, differences between control and flight groups had disappeared by day 7. Cytogenetic analysis of flight seeds showed an increased frequency of aberrant cells for all durations of exposure to space, with greatest numbers of aberrations found in seeds hit by ions. Frequency of aberration increased with flight duration. To a lesser extent this was also true of control seeds, which may be attributed to natural aging. Cells with multiple chromosome breaks occurred most frequently in seeds hit by heavy ions and exposed to space for 201 and 457 days. Fewer multiple aberrations were found in unhit flight seeds, with fewer still in control seeds.

There was a linear relationship between the absorbed dose of radiation and the observed effects (number of aberrant cells, cells with multiple chromosome breaks). The highest frequency of aberrant cells occurred in flight seeds irradiated with a dose of 63.4 mGy. The data obtained indicate that the biological effectiveness of heavy ions is considerably greater than would be predicted on the basis of absorbed dose and fluence. The dose-effect curves for the frequency of aberrant cells were parallel for hit and unhit seeds; however, this was not the case for the

parameter of frequency of cells with multiple chromosome aberrations. In the range of doses of 16 - 63.4 mGy, the slope of the curve for hit seeds was greater than for unhit seeds. This suggests that as flight duration increases, the frequency of multiple damage due to direct effects of heavy ions with higher charges also increases. In the Bioblok-3 experiment, with durations of 201 and 457 days, only heavy ions with charges $Z > 16$ were counted.

The authors conclude that their data show that the effects that were obtained result from direct hits by individual heavy nuclei of galactic cosmic radiation. However, both current and previous work has noted similar effects in seeds not hit by heavy ions. Possible causes of these changes may be particles with $Z < 16$, which were not recorded, or nonionized mechanisms, such as acoustic and impact waves, forming as a result of heating and changes in the aggregate state of the substance in the particle track. It was recommended that further studies be devoted to the effects of multicharged ions (produced by an accelerator) with known physical parameters of effect and under controlled conditions, and also to investigation of nonionized mechanisms underlying formation of primary radiobiological effects.

Table: Cytogenetic analysis of lettuce seeds after exposure on Salyut-6 and Salyut-7

Exposure duration	Group	# seeds	Aberrant cells, %	Cells with multiple aberrations, %	Number of aberrations per aberrant cell
40	Control	54	2.23 ± 0.23	0.23 ± 0.08	1.10
	Flight:				
	Not Hit	310	4.20 ± 0.13	0.31 ± 0.04	1.09
	Hit	267	4.28 ± 0.12	0.50 ± 0.04	1.06
66	Control	33	1.66 ± 0.32	0	1.00
	Flight:				
	Not Hit	31	1.77 ± 0.37	0.07 ± 0.07	1.04
	Hit	40	3.80 ± 0.44	0.26 ± 0.12	1.07
123	Control	20	2.00 ± 0.55	0	1.00
	Flight:				
	Not Hit:	125	3.21 ± 0.35	0.15 ± 0.08	1.06
	Hit	62	4.97 ± 0.55	0.26 ± 0.13	1.13
201	Control	120	3.94 ± 0.28	0.32 ± 0.08	1.11
	Flight:				
	Not Hit	230	5.56 ± 0.39	0.50 ± 0.12	1.09
	Hit	534	8.40 ± 0.25	1.40 ± 0.11	1.25
457	Control	48	4.90 ± 0.76	0.61 ± 0.27	1.12
	Flight:				
	Not Hit	75	12.52 ± 1.21	1.22 ± 0.40	1.11
	Hit	169	15.15 ± 0.87	2.61 ± 0.39	1.23

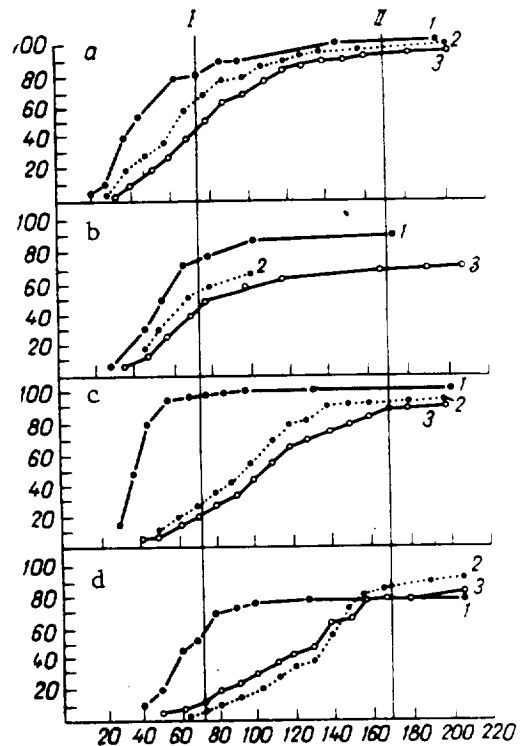
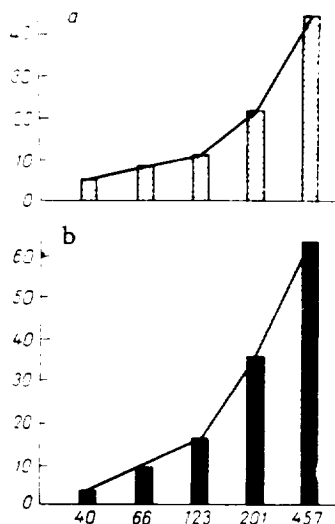


Figure 1: Change in the magnitude of fluence (a) and dose (b) during exposure of cells on Salyut-6 and -7

Abscissa: duration of exposure (days); ordinate: a - fluence (number of particles per cm²); b - dose (mGy)

Figure 2: Dynamics of germination of seeds in a "monolayer" after exposure to space for 40 (a), 66 (b), 201 (c), and 457 (d) days

Abscissa: germination time (hours); ordinate: germination rate (%). I - 3 days; II - 7 days; 1 - control; 2- unhit flight seeds; 3 - hit flight seeds

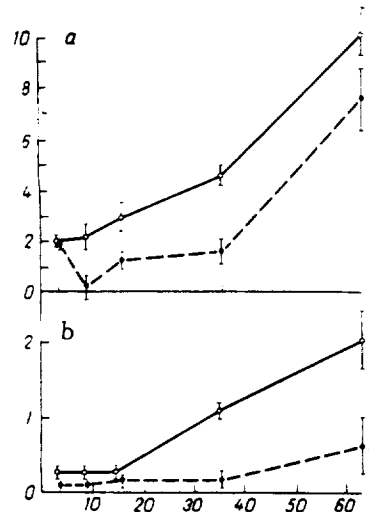


Figure 3: Frequency of aberrant cells (a) and cells with multiple aberrations (b) in lettuce seeds exposed to space as a function of absorbed dose. Rate of spontaneous mutation has been subtracted.

Abscissa: dose (mGy); ordinate: a - aberrant cells (%); b - cells with multiple aberrations (%). 1 - seeds not hit by heavy ions; 2 - seeds hit by heavy ions.

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

PAPERS:

P1202(27/90)* Turchaninova VF, Yegorov AD, Domracheva MV.

Central and regional hemodynamics on long-term space flights.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 19-26; 1989.

[20 references; 6 in English]

Cardiovascular and Respiratory Systems, Hemodynamics, Central, Regional
Humans, Cosmonauts
Space Flight, Long-term, Salyut-6, Salyut-7, Exercise

Abstract: This paper describes results of study of central and regional hemodynamics in cosmonauts on long-term flights using the method of tetrapolar impedance plethysmography. The instrument utilized, the "Reograf-2," not only generated a rheographic curve but also produced a calibrated signal proportional to the constant component of impedance. Both signals were transmitted on the same channel, minimizing possible measurement errors. Impedance plethysmograms of the forearm and calf, right and left hemispheres (using frontal mastoid leads); and the torso, were recorded. Measurements were made of resting subjects, and subjects exposed to graded physical exercise (minute 1 after 5 minutes of pedalling on a bicycle ergometer with loading of approximately 800 kgm/min). Impedance plethysmograms were recorded from the trunk. Impedance plethysmograms of the head were recorded during LBNP (-25 mm Hg for 2 minutes, -35 mm Hg for 3 minutes) for all cosmonaut subjects and additionally of the trunk for members of the Salyut-6-Soyuz, and Salyut-7-Soyuz crews. Cardiac stroke volume and circulatory minute volume were determined from the impedance plethysmogram of the body (shoulder - shoulder) according to the formula $SV = \Delta R / R \cdot P$, in which R is baseline resistance, ΔR is the change in resistance, and P is body weight (in grams). The following parameters were computed from the regional impedance plethysmograms: 1) pulsed blood filling index (PBFi), the ratio of the variable and constant components of impedance in the appropriate region, $P: PBFi = \Delta R / R = A_x / K \cdot 10 \cdot 10^{-4}$, where A_x is the amplitude of the major plethysmogram wave, and K is the amplitude of the calibrated signal; 2) duration of the rapid rise in the anacrotic portion of the impedance plethysmogram curve, primarily reflecting tonus of precapillary vessels (small arteries and arterioles); diastolic index of the ratio of the amplitude of the dichrotic peak to the amplitude of the major wave of the impedance plethysmogram, reflecting outflow of blood from the area under consideration and tonus primarily of the postcapillary vessels.

[Note: Number or identity of cosmonaut subjects and range of flight duration are not directly specified in this article. Evidently long-term flights were accomplished on Salyut-6 and -7 and lasted 65-237 days.]

At rest on short-term flights (typically on day 2-3 of flight), heart rate was virtually unchanged, stroke and circulatory minute volumes decreased nonsignificantly (by 8 and 13%, respectively). On long-term flights, heart rate increased somewhat (from 60 to 66 beats/min in month 2-3), while stroke and minute volume were unchanged. Lack of expected change in stroke volume is attributed to initiation of reflex responses from receptors in the cardiopulmonary region. On long-term flights, heart rate increased in minute 1 after exercise: from 59 to 91 beats/min in month 1; and from 68 to 96 beats/min in months 2-8 (preflight from 68 to 97). Stroke volume in flight increased by 5% (not statistically significant) in month 2-8 of flight (preflight by 20%), while minute circulatory volume increased by 55-58% (preflight 79%). These results suggest that during space flight the mechanism determining minute circulatory volume in response to exercise is different from that on Earth. Preflight the increase in this parameter is attributable both to heart rate and to stroke volume,

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

while inflight the role of the chronotropic function of the heart increases. These results suggest that in flight after exercise there is greater blood pooling in the lower extremities than on Earth.

In response to LBNP, heart rate increased from 68 to 82 beats/minute inflight compared to an increase from 63 to 77 beats/minute preflight. Response of minute and stroke volumes were virtually unchanged.

On short-term flights there was a 22% increase in pulsed blood filling in the forearms by 22% and a statistically significant 29% decrease in this parameter in the calves. There was a decrease in tonus of large vessels in both areas, more pronounced in the calves. Pre- and postcapillaries of the forearm underwent dilation, while fine vessels of the calves underwent only insignificant changes. On long-term flights, pulsed filling in the forearm was virtually unchanged from preflight values, while filling in the calves decreased by 25-26%. At the same time, tonus of small vessels in the forearms decreased by 32-40% and that of large vessels of the calf by 17-19%. Differences between corresponding parameters of the forearms and calves decreased considerably in weightlessness.

On short-term flights there was a general absence of regular changes in parameters of blood filling and tonus of brain vasculature. On long-term flights pulsed blood filling decreased in the left hemisphere in months 2-8 by 10% and tended to increase in the right hemisphere, leading to a moderate level of interhemisphere asymmetry. At the same time the tonus of the pre- and postcapillaries decreased, leading to significant decrease in diastolic and diastolic indices in the impedance plethysmogram. Venous waves synchronous with the atrial complex on the EKG were noted, especially on the right. These phenomena indirectly suggest impeded venous outflow from the skull. The majority of cosmonauts displayed signs of vasodilation in the head, which may serve to improve outflow and prevent further venous engorgement. When LBNP (-35 mm Hg) was applied both pre- and inflight, parameters of pulsed blood filling decreased in the brain. No differences were noted in pre- and inflight tests. Tonus of small vessels of the head did not change significantly in response to LBNP, either preflight or during week 1 of flight. On long-term flights tonus of the small vessels of the head, which was generally reduced, increased in response to LBNP up to preflight levels. Thus LBNP has a normalizing effect on these vessels. Mean values of blood filling of brain vessels during LBNP generally exceeded preflight levels. During months 2-8 of flight, tonus of large vessels and postcapillaries on the right increased. Inflight application of LBNP decreased individual differences in these parameters. The authors conclude that the changes observed in central and regional hemodynamics during space flight result from restructuring of the general hemodynamic status under conditions of weightlessness and vary as a function of flight duration and location of the area studied with respect to the heart. These changes are considered to reflect adaptation to space flight factors and suggest that the circulatory system still retains adaptive potential on flights lasting up to 237 days.

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Table: Deviations (in %) of mean parameters of hemodynamics of the head (basin of the internal carotid artery) in response to LBNP (-35 mm Hg) during short- (7 days) and 65- to 237-day longterm space flights as compared to preflight values

Parameter	Short-term flight	Long-term flights	
		Month 1	Months 2-8
Pulsed blood filling of the head			
right	5	16	14
left	18	5	-18
Tonus of large vessels			
right	1	4	15
left	-3	2	7
Tonus of capillaries			
right	-3	33	13
left	-8	41	9
Tonus of postcapillaries			
right	-17	3	14
left	-14	-4	-1

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

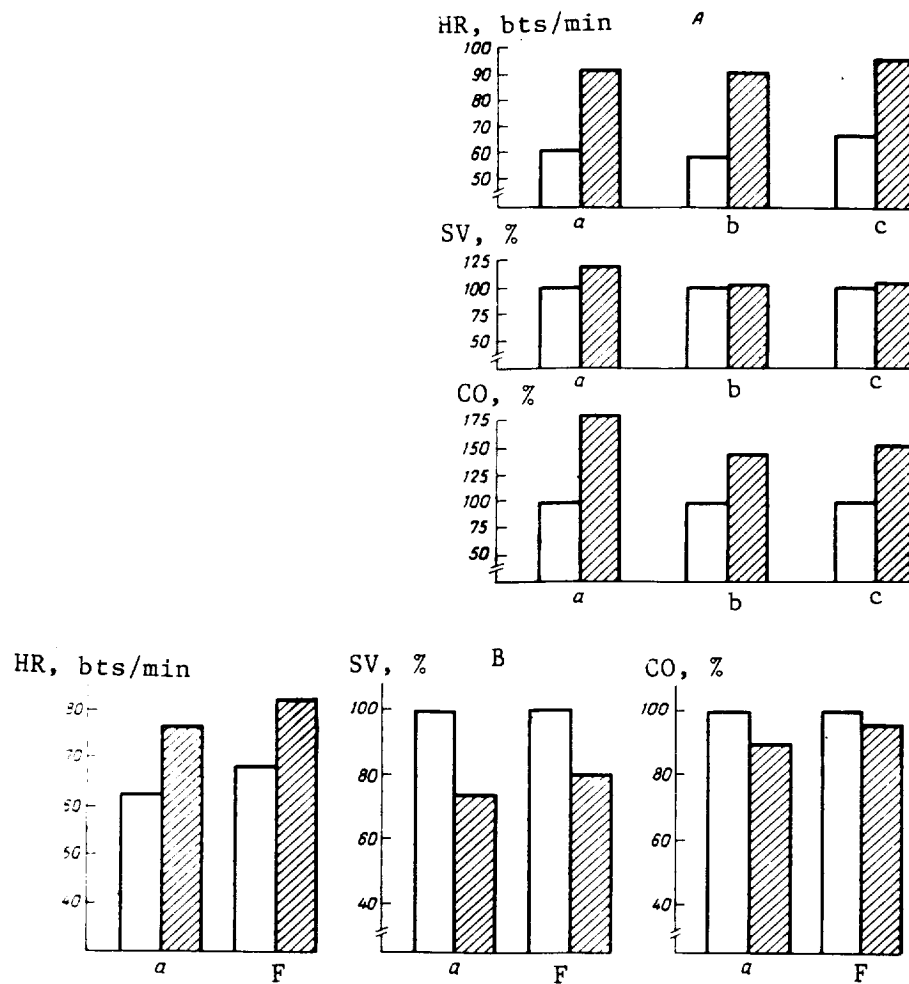


Figure 1: Change in mean values of heart rate (HR), stroke volume (SV), and cardiac output (CO) before and during long-term space flights (65-237 days)

A- in response to graded physical exercise test (minute 1 of recovery); b- in response to LBNP (-35 mm Hg)

Here and in Figure 4: white bars - before the test; hatched bars - after the test. a - preflight, b - month 1 inflight; c - month 2-8 of flight F - flight

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

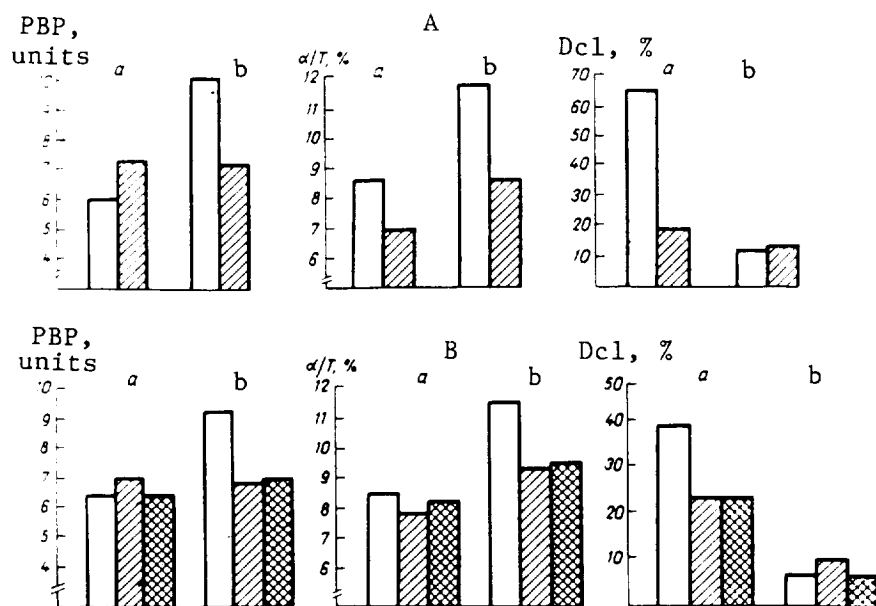


Figure 2: Change in mean value of pulsed blood filling parameter (PBP), tonus of large vessels (α/T) and precapillaries (Dcl) of vessels of the forearm (a) and calves (b) at rest and during short-term - 7 day (A) and long-term - 65-237 day flights (B)

A: white bars - preflight, hatched bars - flight. B: white bars - preflight; hatched bars - month 1 of flight; cross hatched bars - months 2-8 of flight

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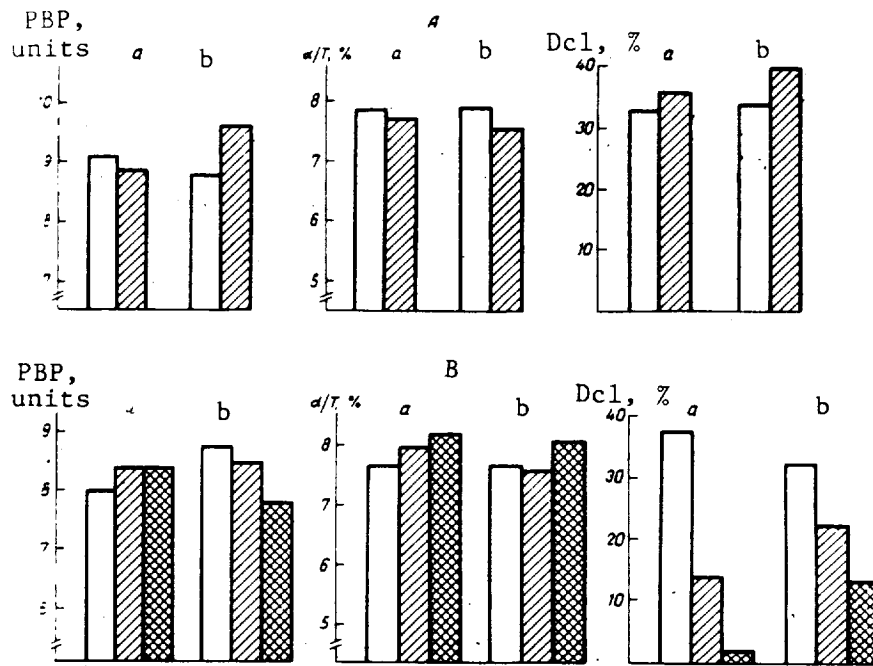


Figure 3: Change in mean value of pulsed blood filling parameter, tonus of large vessels (α/T) and precapillaries (Dcl) of vessels of the head (basin of the internal carotid artery, a - right hemisphere; b - left hemisphere) at rest and during short-term - 7 day (A) and long-term - 65-to 237-day flights (B)

Legend same as Figure 2.

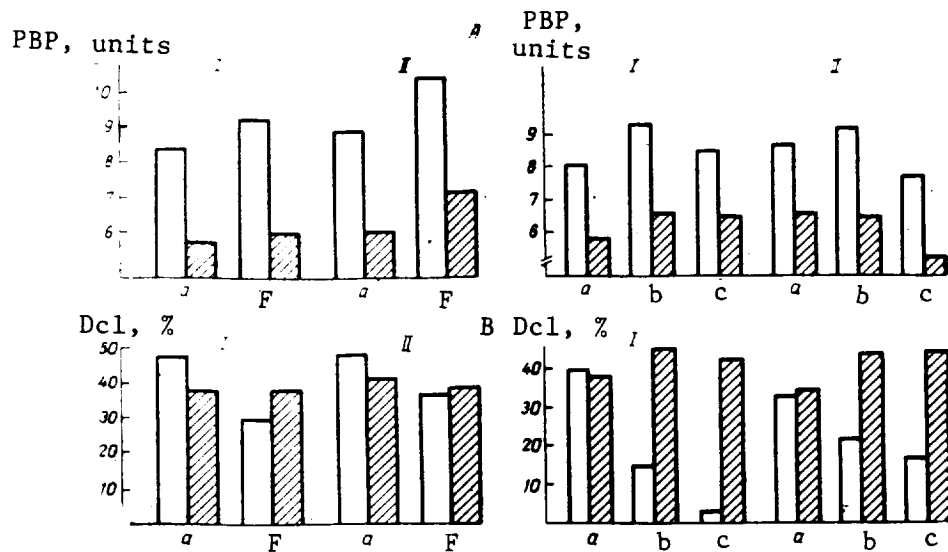


Figure 4: Change in mean value of pulsed blood filling parameter, tonus of large vessels (α/T) and precapillaries (Dcl) of vessels of the head (basin of the internal carotid artery, I - right hemisphere; II - left hemisphere) in response to LBNP (-35 mm Hg) before and during short-term - 7 day (A) and long-term - 65-to 237-day flights (B)

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

P1208(27/90)* Kuznetsov VI.

Cardiac contractility of guinea pigs exposed to long-term continuous stress.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 42-47; 1989.

[18 references; 3 in English]

Cardiovascular and Respiratory Systems, Cardiac Contractility

Guinea Pigs

Psychology, Stress

Abstract: Experiments were performed on 52 female guinea pigs. Subjects were stressed by placing them in groups of 3-4 in confining cages for periods of 60 and 100 days. Matched control groups were used. Food and water were not restricted. During the first stage of the experiment cardiac contractility was measured in anesthetized animals after opening of the chest cavity. Pressure in the left ventricle was recorded using an electromanometer. To test resistance to isometric loading, the aorta was occluded for 30 seconds, with pressure recorded at seconds 5 and 25. The pressure curve was used to compute the following parameters: heart rate, developed pressure, maximal rate of contraction and relaxation of the left ventricle. Rate pressure product was computed as the product of heart rate and developed pressure, while the index of structural function was considered the product of heart rate and developed pressure per unit dry mass of the myocardium of the left ventricle. During the second stage, the heart was rapidly removed from anesthetized guinea pigs and placed in an ice-cold normal saline solution until contraction stopped. The heart was then perfused with an oxygenated bicarbonate Krebs-Henselate buffer, with pH of 7.3-7.4 and temperature maintained at 34°C. A metal cannula was inserted in the left auricle, through which the solution entered the left ventricle. The aortal cannula was attached with a glass tube with outlets every 10 cm allowing graded estimate of aortal resistance. Studies of the hearts of untreated and chronically stressed guinea pigs were performed under conditions of spontaneous heart rate and with aortal pressure fixed at 80 cm H₂O. The muscle fibers of the ventricle were subjected to stretching by increasing pressure in the left auricle from 5 to 25 cm H₂O. Data were tested using Student's t.

After 60 days of stress, the body weight of the guinea pigs was depressed by 12%, and after 100 days by 14%. The dry mass of the left ventricle had not changed significantly after 60 days of stress, but had decreased by 10% after 100 days. Relative mass of the ventricle did not differ from controls. When cardiac contractility was studied with the heart in the body, it was found that after 60 days of stress, heart rate and intraventricular pressure did not differ from control, although developed pressure showed a tendency to increase, causing the parameter of intensity of contractile function to increase by 29%. Maximal rates of contraction and relaxation were unaltered, while the parameter of intensity of structural function was elevated by 39%. In second 5 after occlusion of the aorta, heart rate, developed pressure, rate pressure product and index of structural functioning were unchanged, while maximal rate of contraction and relaxation had increased by 34 and 35%.

After 100 days of stress, all the above parameters previously undergoing changes had returned to control values at rest and at second 5 of occlusion. The exception was index of structural functioning which was elevated by 32 and 27% at rest and second 5 of occlusion. This effect was associated with a slight increase in heart rate and a slight decrease in dry mass of the left ventricle.

Experiments on isolated hearts from animals subjected to 100 days of stress showed higher minute volume in hearts of stress-adapted animals in response to increasing perfusion of the heart (see Figure). The authors interpret these results as indicating that the isolated hearts of guinea pigs undergoing 100 days of stress not only do not lose the capacity to respond to

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

increased filling pressure by increasing minute volume, but even at some pressures show increased output relative to controls. The authors conclude that continuous 60- to 100-day stress leads to development of adaptive processes in the heart, manifested in increased contractile function of the myocardium in mature animals that (unlike rats) have ceased to grow. The effects of adaptation can be observed at the level of the organism as a whole as well as in isolated hearts, suggesting that adaptation involves central mechanisms of regulation, as well as autoregulation.

Table 1: Change in myocardial contractile function in guinea pigs undergoing long-term chronic stress

Table 2: Change in minute volume of isolated hearts in control and stress-adapted animals at various loading levels

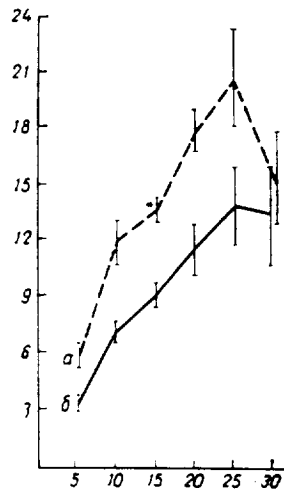


Figure: Filling pressure and minute volume in experiments on isolated hearts of control guinea pigs (a) and those undergoing a 100-day period of stress

Abscissa - filling pressure in the left ventricle (in cm H₂O); ordinate - minute volume (in ml/min per 1 kg moist tissue of the left ventricle. * - significant differences

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

P1226(27/90) Beketov AI, Konyayeva Yel.

Circulation and oxygen pressure in the brains of alert and anesthetized rabbits in a head-down tilt position.

Fiziologicheskii Zhurnal SSSR im I.M. Sechenova

75(11): 1548-1553.

Authors' affiliations: Medical Institute of Crimea, Simferopol; Sechenov Institute of Evolutionary Physiology and Biochemistry, Leningrad

Cardiovascular and Respiratory Systems, Circulation, Oxygen Pressure, Brains
Rabbits, Alert, Anesthetized
Head-Down Tilt

Abstract: The goal of this work was to analyze changes in local blood flow and oxygen pressure in various regions of the cerebral cortex and total brain blood flow in alert and anesthetized rabbits in head-down tilt position. Subjects were 23 alert and 4 anesthetized rabbits. Changes in local and total brain blood flow were measured using the hydrogen clearance method with a nanovolt ammeter and a loop oscillograph, oxygen pressure was measured polarographically. Animals breathed hydrogen in a 5% mixture with air for 1 minute. Specific blood flow rate was computed using the "initial slope" method and expressed in ml/100 g/min; oxygen pressure was expressed in percent of baseline. Local blood flow and PO₂ were measured using platinum needle electrodes, inserted through holes drilled in the skull of the parietal, frontal, occipital, and left and right temporal lobes of the cerebral cortex. Overall brain blood flow was computed from venous outflow from the skull and PO₂ in venous blood was measured using electrodes in contact with the dura mater in the confluence of the venous sinuses. In the chronic experiment electrodes were implanted 2 weeks before the experiment and, in the acute experiment performed on anesthetized animals, inserted immediately before the experiment. Blood pressure was measured in the short-term experiment in the femoral artery, and in the long-term one through an indirect method based on the pulse in the femoral artery. EKGs were also recorded. Blood flow was measured every 5-10 minutes in the initial position, during head-down tilt (-45° for 1 hour), and after return to the horizontal position. At these same intervals changes in PO₂, blood pressure, and EKG were also recorded.

In alert animals during head-down tilt blood flow changed in different ways in different parts of the cortex. Immediately after the animals were placed in this position, blood flow increased insignificantly in the parietal, left and right temporal, and decreased insignificantly in the occipital lobes. After 10 minutes it significantly increased in the right temporal and frontal areas of the cortex and decreased significantly in the left temporal area. No change occurred in the parietal and occipital areas. After 30 minutes and continuing until the end of the tilt period most regions of the cortex displayed decreased blood flow. At the onset of head-down tilt, there was a 55% increase in blood flow in the confluence of venous sinuses of the brain, which was replaced after 10 minutes by a decrease (to 77% baseline). Blood pressure changes also underwent two phases: increase to 108% at minute 5 and an insignificant decrease toward the end of the tilt period. No change in EKG was noted, although heart rate gradually decreased.

After the animals were moved into a horizontal position, there was a significant increase in blood flow in the parietal and frontal cortex and a statistically insignificant increase in the occipital and left temporal areas. Blood flow in the right temporal area decreased significantly, while blood flow in the sinus confluence increased. Change into the horizontal position led to a rapid but short-lived hypertensive reaction. When 30 minutes had elapsed after termination of head-down tilt, the majority of parameters (except for the parietal region, were below baseline). Onset of head-down tilt led to decreased PO₂ in all regions of the cortex and in the confluence of the brain sinuses. After return to horizontal position, PO₂ in the parietal and left temporal areas rapidly returned to baseline and then decreased again. After 30 minutes, PO₂

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remained below normal in the cortex and had decreased still further in the confluence of the sinus.

In anesthetized animals onset of head-down tilt led to changes in different directions in the various regions of the cerebral cortex. In the parietal and temporal regions there was first a short-term, insignificant decrease in blood flow and then an increase lasting 10-20 minutes, followed by another decrease. In all other areas and in the confluence of the sinuses there was a decrease in blood flow throughout the period of head-down tilt.

The authors conclude that the most extreme changes in systemic and organ hemodynamics occur during the first few minutes after change of position. The most characteristic and pronounced fluctuations in blood flow and pressure are seen during these periods and may be considered the initial response to postural factors. Subsequent changes in hemodynamics may be a result of interaction between the disturbing element and compensatory mechanisms serving to increase functional stability of the brain circulation system. Thus, stimulating compensatory mechanisms through various measures, including drugs, may facilitate adaptation of cerebral hemodynamics to extreme conditions.

Figure 1: Blood flow in various regions of the brain in alert rabbits during head-down tilt

Figure 2: Changes in blood flow rate in various regions of the brain in alert and anesthetized rabbits during exposure to head-down tilt

PAPER:

P1203(27/90)* Prodan NG (USSR) and Baranska V (Poland).

Morphological research on the adrenal glands of rats after flight on COSMOS-1667.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 27-30; 1989.

[15 references; 1 in English]

Endocrinology, Adrenal Glands, Morphology

Rats, Males

Space Flight, COSMOS-1667

Abstract: The adrenal glands of 7 adult male rats of the Wistar line sacrificed 4-8 hours after completion of a 7-day space flight and 7 rats of a vivarium control group were cleaned of fat tissue, weighed, and fixed. After fixation the entire gland was embedded in paraffin. Sections 4-5 μ m thick were prepared from the central portion of the gland (with a maximum of cortical substance) and stained to allow differentiation of cells secreting adrenalin (A-cells) and noradrenalin (N-cells). Measurements were made of the relative amounts of cortical and medullary substance, size of cytoplasm and nuclei of cells in different zones of the cortex; the area occupied by the A- and N- cells, size of nuclei and volume density of medullary cells. An image analyzer was utilized for measurement. Data were tested using Student's t, with a $p < 0.05$ significance level.

No differences were found between flight and control animals with respect to adrenal weight and volume of cortical and medullary substance. Histological examination did not reveal significant changes in flight animals, with the possible exception of a slight narrowing of the glomerular zone. Cortical hyperemia was noted, with capillaries dilated in the reticular and fascicular zones. Judging by vacuolization of the cytoplasm, there was a slight decrease in lipids in flight rats. There was a slight but significant increase in the areas of cytoplasm and nuclei in the glomerular zone, without the ratio of the two being altered. Size of nuclei of cells in the fascicular zone increased. In medullary substance, area occupied by N-cells decreased by 28% in flight rats, while area occupied by A-cells was unchanged. In flight rats size of medullary cell nuclei decreased, while the volume density of the nuclei increased considerably.

The authors conclude that the stress response engendered by short-term exposure to weightlessness was slight, as evidenced by absence of hypertrophy of the cortical substance overall and in the fascicular zone. Increase in cell size in this zone evidently resulted from shifts in fluid electrolyte balance during early exposure to space. The results of morphological study of the medullary substance suggest that weightlessness does not act as a stressor of this component of the sympathetic system, since there is no sign of hypertrophy and indeed area occupied by N-cells and nuclei of medullary cells was diminished.

Table 1: Weight of the adrenal glands and relative amounts of cortical and medullary substance in rats in the flight and vivarium control groups

Condition	Adrenal weight, mg per 100 g body weight	Relative Volume, %	
		cortical substance	medullary substance
Flight	12.7 \pm 0.36	83.62 \pm 0.77	16.38 \pm 0.77
Control	12.8 \pm 0.48	84.70 \pm 0.70	15.30 \pm 0.70

Differences are not statistically significant.

ENDOCRINOLOGY

Table 2: Results of morphometric studies of the cortices of rats after a 7-day space flight on biosatellite COSMOS-1667

Parameter	Control Group	Flight Group	p
Glomerular zone			
Volume of cell cytoplasm, μm^3	201.51 \pm 11.7	223.91 \pm 12.96	<0.05
Volume of cell nuclei, μm^3	85.50 \pm 1.69	94.96 \pm 1.69	<0.05
Ratio of nuclei and cytoplasm, %	42.43 \pm 1.62	42.41 \pm 1.70	>0.1
Fascicular zone			
Volume of cell cytoplasm, μm^3	324.10 \pm 20.97	310.7 \pm 18.46	>0.1
Volume of cell nuclei, μm^3	114.60 \pm 1.71	139.97 \pm 2.97	<0.05
Ratio of nuclei and cytoplasm, %	35.36 \pm 1.76	45.05 \pm 1.72	<0.05
Reticular zone			
Volume of cell cytoplasm, μm^3	261.49 \pm 20.63	258.67 \pm 14.55	>0.1
Volume of cell nuclei, μm^3	88.90 \pm 2.83	94.14 \pm 2.14	>0.1
Ratio of nuclei and cytoplasm, %	33.99 \pm 1.59	36.39 \pm 1.22	>0.1

Table 3: Results of morphometric investigation of medullary substance of adrenal glands of rat after space flight on biosatellite COSMOS-1667

Parameters	Total area, mm^3		Volume of cell nuclei, mm^3	Volume density of nuclei, %
	A-cells	N-cells		
Vivarium control	0.700 \pm 0.002	0.070 \pm 0.001	144.70 \pm 3.10	6.48 \pm 0.41
		p<0.05	p<0.05	p<0.05
Flight	0.700 \pm 0.002	0.050 \pm 0.002	128.51 \pm 2.37	16.87 \pm 1.03

P1211(27/90)* Yangalycheva EA.

Hypothalamus/pituitary neurosecretory system in rats exposed to high-altitude hypoxia.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 54-62; 1990.

[21 references; 3 in English]

Endocrinology, Hypothalamus, Pituitary; Neurophysiology, Neurosecretory Apparatus;

Morphology

Rats

Adaptation, Hypoxia, High-Altitude

Abstract: Morphological changes were studied in the hypothalamic/pituitary neurosecretory system in 37 white rats during a period of adaptation to high altitude (3200 m above sea level) conditions during the summer. Animals were sacrificed for study on day 3 (n=6), 10 (n=4), 20 (n=6), 30 (n=5), 40 (n=6), and 60 (n=4) of adaptation. The hypothalamus and the pituitary were isolated and fixed in Bouin's fixative. Frontal and sagittal sections were laid out in an incremental series and stained to reveal nucleic acids. The functional status of the system was estimated from a number of quantitative and semiquantitative parameters. Functional significance of migration of Gomori-positive granules of the neurosecretory substance was computed by formula from parameters, such as the concentration of neurosecretory substance in neurosecretory cells, the supraoptic nucleus, and supraoptic terminals, and secretion of type 1a neurosecretory substance by the supraoptic nucleus.

The topography and form of the glial nuclei in the supraoptic nucleus and neurohypophysis revealed clear phase-related differences: if the nucleus was enlarged, then the number of spherical nuclei (active phase of adaptation) was elevated, and vice versa. Close structural interactions among glial nuclei, neurosecretory cells and their axons, and terminals in the neurohypophysis determine the characteristics of the functioning of the hypothalamus/pituitary neurosecretory system under conditions of high altitude.

Table 1: Major characteristics of the supraoptical nuclei of rats adapting to high altitude hypoxia

Table 2: Changes over time in neurosecretory substance in the neurohypophysis in rats during adaptation to high altitude

Table 3: Statistical characteristics of the state of the supraoptic nucleus and neurohypophysis of rats under conditions of high altitudes

Figure 1: Hypothalamus-pituitary system of rats undergoing adaptation to high altitudes

Figure 2: Dynamics of morphological changes in the neurohypophysis of rats during adaptation to high altitudes.

P1219(27/90)* Zagorskaya YeA.

Endocrine response to low frequency electromagnetic fields of continuous and intermittent generation.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 4-15; 1990.

[126 references; 54 in English]

Endocrinology, Endocrine Response

Humans and Animals, Review Article

Radiobiology, Low-Frequency Electromagnetic Fields, Constant, Intermittent

Abstract: This work reviews recent literature on the biological effects of exposure to low-frequency continuous and intermittent electromagnetic fields, especially on the endocrine system. A number of works have demonstrated that the hypothalamus is one of the most sensitive organs to electromagnetic fields, and that the hypothalamus-hypophysis region is one of the first portions of the body to react to such stimulation. Even with weak intermittent electromagnetic fields and short exposure concentration of ACTH in the pituitary has been shown to increase substantially after exposure. Morphological study of the adenohypophysis of rats repeatedly exposed to intermittent electromagnetic fields revealed signs of activation or strain on the functions of the gonadotropic cells and those that synthesize thyrotropin. Exposure to a low frequency constant electromagnetic field leads to cyclic changes in the posterior lobe of the hypophysis, supraoptic nucleus, hypothalamus and adrenal cortex, with alternation of elevated and depressed hormonal activation. These effects are interpreted as indicating decreased regulatory potential of the neurohumoral and pituitary-adrenal gland system.

Electromagnetic fields have been found to have significant effects on melatonin, a regulator of many endocrine reactions. These effects are associated with disrupted circadian rhythms. After chronic exposure to certain intermittent fields the cortical layer of the adrenal gland increased in width due to cells of the fascicular zone. 11-OCS was found to increase in the blood of rats after exposure to a constant electromagnetic field. Response of the adrenal gland in mice varied as a function of duration of exposure to the field. There was some evidence of adaptation to constant long duration exposure. Effects were found to vary qualitatively as a function of field strength and other conditions of exposure.

Humans exposed to low frequency constant magnetic fields close in field strength and frequency to that of a natural magnetic storm displayed changes in the functional activity of the pituitary/adrenal system. Differences were noted between effects of single and multiple exposures and individual differences were marked. It seems likely that long-term exposure will diminish the reserve capacities of the systems.

Many studies have demonstrated that the testes of animals are sensitive to the fields under discussion. Changes found have included hemodynamic disturbances, disruption of cytoarchitecture of the spermatogenic epithelium, and depressed spermatogenesis. Morphological change evoked by repeated or chronic exposure did not always normalize, even after 1-2 months. Human studies have shown increased concentrations of testosterone after exposure to such fields. Results of exposure to these fields on reproductive capacities of animals have been contradictory, possibly due to differences in field intensities or other discrepancies in conditions. Results concerning effects on female reproductive function have also been contradictory.

Animal results have indicated that low frequency constant magnetic fields can affect the thyroid glands, with both depression and activation of thyroid activity noted under different conditions of field strength, exposure, and delay. Human results have included increased levels of

ENDOCRINOLOGY

thyrotropin, and free and total thyroxin, as well as decrease in thyroxin in blood. Some of these effects have been relatively long-lasting.

Data on pancreatic effects of low frequency magnetic fields are very sparse. Insulin insufficiency has been reported in rats.

Reported effects on the sympathetic adrenal system have included decreased adrenalin in the adrenal gland, decreased noradrenalin in the brain, hypertrophy of chromaffin cells in the adrenal cortex, and decreased noradrenalin in the hypothalamus.

The authors conclude that these data attest to the sensitivity of the endocrine system to exposure to low-frequency constant electromagnetic fields. Evidently, alteration of the functional activity of the pituitary-adrenal, pituitary-thyroid, and sex hormone systems, and of the pancreas, which are regulated by higher levels of the neuroendocrine systems may change as a function of intensity and duration of exposure, sensitivity of the gland, and individual sensitivity. Intermittent electromagnetic fields of the same induction and frequency have greater biological effectiveness than constant ones. The response evidently is not specific and is similar to that noted in the general adaptation syndrome. Duration of symptoms of endocrine stress suggest that complete adaptation does not occur to this factor. It is possible that the testes are more sensitive than the ovaries to the effect of low-frequency constant magnetic fields, but there is insufficient data to support this conclusion. The pancreas is highly sensitive to constant electromagnetic fields with 20mT, 50 Hz, but effects of fields with other parameters have not been studied.

Exposure to constant magnetic fields with specially selected parameters has been tested as a means to increase general resistance to various adverse factors. Such exposure has been found to help rats withstand hypokinesia. In clinical practice, continuous and intermittent low-frequency electromagnetic fields have been used therapeutically for ischemic heart disease, high blood pressure, and inflammation of the fallopian tubes and ovaries.

It has been demonstrated that exposure to low-frequency electromagnetic fields is associated with decrease in rate of catabolic processes, increase in anaerobic glycolysis, disruption of the permeability of cell membranes, and development of hypoxia in the cells of certain tissues. Repeated exposure had been associated with changes in nucleic acid and nitrogen metabolism in various tissues. It has not been determined whether the initial effects of these fields occur at the level of the whole organism through regulatory structures of the hypothalamus, pituitary, and adrenal glands, or directly at the cellular level, through the sensitive cell membranes and mitochondria. There is no appropriate model of the effects of low-frequency electromagnetic fields on the nervous system.

According to the author, the data he cites suggest that, by virtue of their primary interactions with the cellular membrane, constant electromagnetic fields can be applied to affect adenylate cyclase and thus alter synthesis of cAMP and/or the response of "secondary mediators." He argues that electromagnetic fields in all likelihood influence the organism through a set of changes at various levels of organization. It is possible that as intensity of the stimulation increases, the key role played by certain mechanisms will increase. He concludes that increase in research on various aspects of hormone-receptor interactions and transmission of hormonal signals to the cell during exposure to low frequency constant magnetic fields will make an important contribution to understanding how this factor operates on biological subjects.

PAPER:

P1225(27/90) Shepotinovskiy VI, Rogoznyaya NA, Mikashinovich ZI.

Activity of digestive enzymes in response to immobilization stress and its pharmacological correction with adrenoreceptor blocking agents.

Patologicheskaya Fiziologiya i Eksperimental'naya Terapiya.

1989(6):49-52.

[10 references; none in English]

Authors' Affiliation: Central Scientific Research Laboratory, Rostov Medical Institute

Enzymology, Digestive Enzymes; Gastrointestinal System

Rats

Adaptation; Immobilization Stress; Pharmacological Countermeasures; Adrenoblockers

Abstract: This experiment was performed on 80 white rats of both sexes. Stress was induced in hungry animals by immobilizing them on their backs for 3 or 24 hours. In another condition, animals were adapted to stress by gradually increasing immobilization for from 15 minutes to 3 hours over the course of 10 days. The α -blocker, pyrroxan (6-[β -(3-Phenylpyrroprolidyl-1') propionyl-benzodioxan-1,4 hydrochloride) in a dose of 1 mg/100 g) and the β -blocker obzidan (Inderal) in the same dose, were administered subdurally to some animals. One group of these subjects was then exposed to 3-hours of immobilization stress, while the other group received no further treatment. The effects of the drugs on intestinal digestion were studied 3 hours after their administration in both groups. Sour milk (30 g) was fed to both groups and after 1 hour enzyme activity of the epithelium of the upper third of the small intestine was measured. Activity of enterokinase was measured in a homogenate of a scraping from the mucous membrane in a ratio of 1:10 of distilled water. Activity of amylase was measured in plasma and expressed in grams of salt hydrolyzed by the enzyme in 1 l of plasma. Activity of the intestinal isoenzyme of alkaline phosphatase was measured in the presence of L-phenylalanine, which is an inhibitor of the intestinal fraction of serum alkaline phosphatase. Isoenzyme activity was expressed in micromoles of inorganic phosphorus per 1 ml plasma after 1 hour of incubation.

Food loading evoked significant activation of amylase in blood serum. Activity of intestinal alkaline phosphatase decreased by a factor of 1.8, and enterokinase by 1.7. Animals exposed to immobilization stress before feeding displayed sharp increases (by a factor of 2) in activity of amylase and enterokinase, interpreted as a part of the general adaptation syndrome and a consequence of induction of adrenal hormone activity. In these subjects, activity of alkaline phosphatase was 1/10 that of intact animals. Increase of immobilization duration to 24 hours led to normalization of enterokinase and alkaline phosphate activity and decrease in amylase activity to a level intermediate between intact and 3-hour stressed animals. The stress adaptation procedure significantly decreased gastric response to stress, but fell short of normalizing it.

The effect of feeding after 3 hours of immobilization can be described as anti-stress. Activity of enterokinase dropped almost to that of intact fed animals. Activity of amylases was less elevated than before feeding and activity of alkaline phosphatase increased by a factor of 9. Evidently the leading role of exogenous food stimulation on digestive processes is maintained after 3 hours of immobilization stress, despite the changes occurring in endogenous regulatory factors.

In intact animals, administration of adrenoblockers altered activity of the enzymes studied. Pyrroxan, which has a selective effect on α -receptors independent of their localization, decreased activity of all enzymes by a factor of 2.4 to 3. Obzidan, a blocker of β -receptors, had a less marked inhibiting effect. When immobilized animals were injected with the drugs, the

stress response of digestive enzymes was virtually eliminated, with the β -blocker obzidan having a greater effect.

The authors conclude that stress leads to a rapid change in activity of intestinal enzymes, which is adaptive in nature. The magnitude of the responses of the digestive system to stress is determined by the state of the central mechanisms of regulation, and also the degree of participation of the enteric? and hormonal systems, which through numerous feedback loops interact with the general hormonal system. Utilization of α - and β - blockers decrease the activation of the adrenergic regulatory system in response to stress and thus alter activity levels of pancreatic and intestinal hormones.

Table 1: Activity of intestinal enzymes in intact and immobilized animals

Table 2: Effects of α - and β -blockers on the activity of enzymes in intact and immobilized rats

PAPER:

P1229(27/90) Kuzicheva YeA, Malko IL.

Abiogenic thermal synthesis of nucleotides in the presence of lunar soil.

Zhurnal Evolyutsionnoy Biokhimii i Fiziologii.

XXV(6):697-701; 1989.

[13 references; 4 in English]

Authors' Affiliation: Institute of Cytology, USSR Academy of Sciences, Leningrad

Exobiology; Abiogenic Synthesis; Thermal

Nucleotides

Lunar Soil

Abstract: This work investigated the biogenic thermal synthesis of nucleotides in the presence of lunar soil and its analogue tholeitic basalt. The lunar soil used had been sampled by the Luna-16 unmanned station from the Sea of Fecundity. The sample was composed of dark gray regolite with particle diameter of approximately 0.2 mm. Chemicals used included labelled uridine 14C, unlabeled uridine-5'-monophosphate, cyclic uridine-2',3'-monophosphate, uridine-5'-diphosphate, uridine-5'-triphosphate disodium salts, ion-exchange tar DEAE-sephadex, sephadex G-10, unpurified snake venom, and tholeitic basalt. Thermal synthesis of nucleotides was conducted using an undescribed method. Solid films were prepared from the solution of uridine 14C and inorganic phosphate in the presence of lunar soil and basalt (and in their absence) on a rotor condenser. A column with a solid film of the reactive medium was evacuated and then placed in a glycerine bath and heated for 2 hours at a temperature of 160°C. The film was dissolved in hot distilled water, the lunar soil and basalt filtered out, and the remainder analyzed. Analysis involved dissolving, initial purification using DEAE-sephadex A-25, selection of the fraction with V_e corresponding to V_e of natural nucleotides, lyophilization, second purification using Sephadex G-10, enzymatic hydrolysis of 5'-bonds, selection of the fractions that did not disintegrate in snake venom, hydrolysis with alkaline phosphatase, and separation on Sephadex G-10. The nucleotides with an elution volume equal to the elution volume of cUMP after two purifications were also incubated with alkaline phosphatase to determine the amount of cyclic derivative they contained. The yield of products formed was computed in terms of initial quantity of nucleoside.

Heating the mixture of uridine and inorganic phosphate in the absence of a substrate led to formation of six synthesis products. The overall yield was 17.8%, and the quantity of uridine not entering into the reaction was approximately 65%. It was assumed that the remaining uridine disintegrated in response to heat. After the first purification it was established that the major products were uridine monophosphates. Further processing revealed that fraction A consisted of two components A_1 and A_2 . A_1 was present in a quantity 3.6% of the total yield, and contained no compounds with natural bonds, which is logical in synthesis of biochemically important substances using abiogenic techniques. Yield of A_2 was 5.6%. It contained 61% cU-2',3'-MP. Fraction B after the second purification was found to be homogeneous and amounted to 4.6% of the total yield. After enzyme hydrolysis with alkaline phosphatase it was found to contain 70% cU-2',3'-MP. Fraction C (2.2% yield) contained 49% U-5'MP and 5% U-2'(3')-MP. Fraction D (yield 1%) contained 10% U-5'-MP and 44% U-2'(3')-MP. In addition, fractions E and F contained traces of uridine and uridine monophosphates.

Performance of thermal synthesis in the presence of basalt and lunar soil significantly decreased the total yields of reactions to 4.15% and 1.62%, respectively. The composition of the reaction products changed too. None of the products contained uridine or uridine monophosphate. In the presence of lunar soil a substance was formed that had the molecular weight of uridine-monophosphate, but contained no natural bonds.

The authors conclude that lunar soil is not inert, and they hypothesize that the absence of biologically important compounds in lunar samples is due partially to the inhibiting effects of lunar soil.

Table: Characteristics of nucelotides synthesized by heating a mixture of uridine and inorganic phosphate in the absence of a substrate and in the presence of basalt and lunar soil

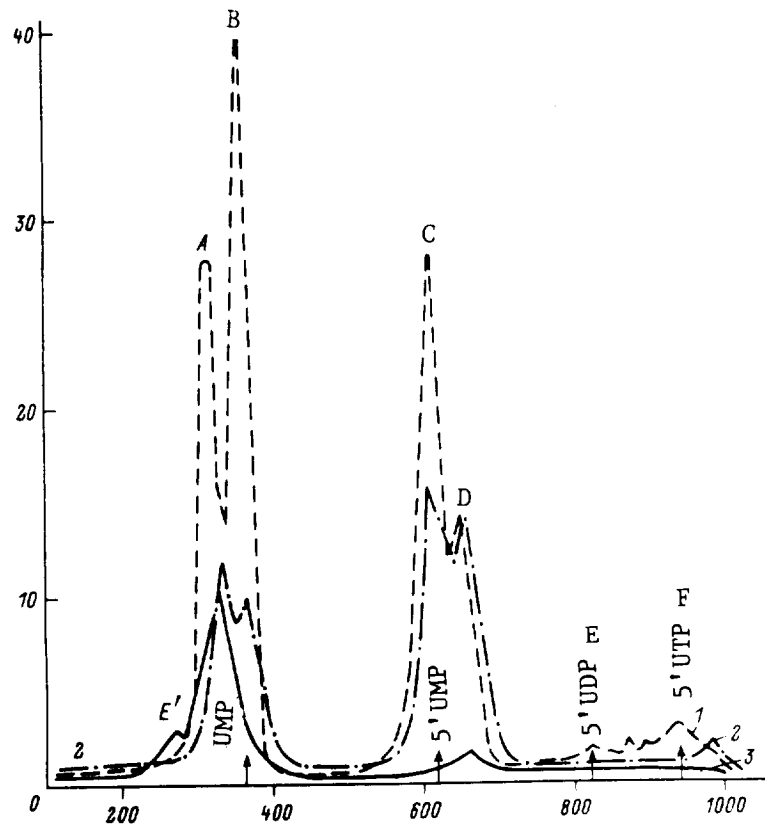


Figure: Chromatogram of nucleotides synthesized by heating uridine and inorganic phosphate without a substrate (1), in the presence of basalt (2), or lunar soil (3)

Column with DEAE-sephadex A=25 (4X28 cm). Elution using a concave gradient from distilled water up to 0.4 M ammonium bicarbonate. Rate of elution 180 ml/hr. Arrows indicate the position of volumes of elution standards. Ratio of uridine $^{14}\text{C} + \text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O} : 10^7 \mu\text{g} + 68 \mu\text{g}$. Ordinate: radioactivity of the fractions ($\text{imp}/\text{min} \cdot 10^{-3}$); Abscissa - elution volume (ml).

PAPER:

P1210(27/90)* Mukhamediyeva LN, Savina VP, Nikitin Yel.

Thermoregulatory responses in humans to moderate levels of hypercapnia.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 51-54; 1990.

[20 references; 7 in English]

Thermoregulatory Response

Humans, Males

Habitability and Environment Effects, Hypercapnia; Pressurized Environment

Abstract: This work examined the effects of moderate hypercapnia on thermal regulation in humans. A total of 20 apparently healthy male volunteers participated in this study. Their thermal status was studied on the basis of measurement of body temperature and skin temperature at 11 points, weighted average mean temperature, mean body temperature and change in heat content. Heat production was estimated on the basis of gas exchange. External respiration was monitored on the "Spirolit-2" apparatus. Acid base equilibrium of arterialized blood was estimated on the basis of partial CO₂ pressure, concentration of base buffer, and base excess. Activity of catalases were measured in blood, as were pyruvate, lactate, and number of erythrocytes. The 10 subjects in the experimental group spent 40 days in a pressurized chamber with a constant level of 1.1-1.6% CO₂ and 19-20% oxygen. Air temperature was maintained at 21-23° and humidity at 50-70%. The control group spent 40 days in an analogous chamber with CO₂ level of 0.2-0.4% and all other conditions the same as for the experimental group.

Body temperature decreased on day 19 of hypercapnia, but this change only reached 0.5° on day 39. Beginning on day 3 of exposure, gas exchange increased, remaining at the elevated level throughout the treatment period. Acid-base balance displayed changes characteristic of compensated respiratory acidosis. The greatest changes in acid-base balance occurred on day 3 of treatment. Number of erythrocytes were virtually unchanged throughout the period, suggesting maintenance of adequate blood oxygen capacitance. Level of lactate in blood decreased significantly starting on day 3 of treatment, possibly suggesting inhibition of glycolysis. As hypercapnia exposure increased, there was a gradual decrease in the heat content of the body before day 19 attributable to decrease of skin temperature and subsequently to core temperature decreases as well. Starting on day 3 of exposure skin temperature decreased in the distal areas of the limbs. Foot temperature decreases were most extreme, and were 2.2° below baseline on day 39. Control subjects also displayed a (less marked) decrease in mean skin temperature, which the authors attribute to hypodynamia. The authors conclude that the results showed that continuous exposure to hypercapnia (1.1-1.6% CO₂) for 40 days in a thermoneutral zone was accompanied by a "cooling" effect along with an increase in heat production starting on day 3. The subsequent significant decrease in lactate in blood was correlated with decreased body temperature ($r=+0.79$). Additional changes included respiratory acidosis, a tendency for excess base buffers to decrease in blood, and disruption of thermal balance as manifested in decreases in body temperature and body heat content, while heat production remained stable. These results do not preclude the possibility that hypercapnia limits thermogenesis at the stage of glycolytic synthesis of ATP.

Table 1: Parameters of the functions of external respiration, acid-base balance of arterialized blood and biochemical parameters of blood in exposure to moderate levels of hypercapnia

Table 2: Thermal parameters of subjects in the control and hypercapnic groups

HABITABILITY AND ENVIRONMENT EFFECTS

Figure: Body temperature, skin temperature, foot temperature and their ratio under exposure to moderate hypoxia

PAPER:

P1215(27/90)* Orlova TA, Kiselev RK.

Use of a ferrocerone test to measure iron reserves under various living conditions.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 77-81; 1990.

[15 references; 2 in English]

Hematology, Nutrition, Blood Iron; Ferrocerone Test

Humans

Hypokinesia with Head-Down Tilt

Abstract: The objective of this work was to develop a methodology for evaluating reserves of iron in the body and to test it on healthy individuals under normal conditions and while undergoing head-down tilt of varying duration. Existing measures for testing iron reserves are either too complex or can only be used when iron deposits are elevated. The authors proposed a method of assessing iron reserves using ferrocerone (a sodium salt of orthocarboxybenzoylferrocene), which is utilized clinically as a supplement to correct iron deficiency. The reasoning was that if the body's supply of stored iron was limited, then iron supplements would be utilized rather than excreted. The particular supplement (ferrocerone) was chosen because it is highly soluble in water and readily absorbable by the mucous membrane of the gastrointestinal tract, enters the bone marrow rapidly, and is well tolerated without side effects. To test dynamics of iron excretion in healthy individuals under conditions of normal activity, a total of 24 healthy young men (group 1) were given ferrocerone in the form of a tablet containing 0.04 g iron in the morning after breakfast. Urine was collected during the following time periods: 09:00-13:00, 13:00-16:00, 16:00-20:00, 20:00-09:00, and iron levels were measured in each sample, on the basis of reaction with bathophenylanthroline. The study of iron levels under conditions of hypokinesia and head-down tilt utilized 20 individuals, 6 of whom spent 50 days in head-down (-6°) hypokinesia while taking folicobalamine, a stimulant of hemopoiesis (group 2). The 14 individuals in group 3 spent 120 days at a head-down angle of -4.5°. Group 2 was studied on days 25 to 15 before treatment, on days 25 and 46 of head down tilt, and days 12 and 28 afterwards. Group 3 was studied before treatment, on days 28, 30, 60-70, and 105-110 during treatment, and 4-5 days after it. Hemoglobin mass was also studied in subjects undergoing hypokinesia.

After individuals living under normal conditions took the dose of ferrocerone, they excreted a total of approximately 50% with urine. In these subjects two temporal patterns of excretion were observed: in one type, excretion peaked during the first 4 hours after taking the drug, and in the other, during hours 4-8. Analysis of the subjects exposed to hypokinesia revealed similar results for the two hypokinesia experiments: 1) before hypokinesia, renal excretion of iron was analogous to the norm 2) during days 25-30 of hypokinesia with head-down tilt, excretion of iron after ingestion of ferrocerone was virtually the same as baseline, while mass of hemoglobin decreased; 3) on day 45 excretion of iron began to decrease, with hemoglobin either increasing slightly or continuing to decrease; 4) on days 65-75 for the 120-day study and day 13 of readaptation for the 50-day study, iron retention was greatest, with 68% of iron administered retained in group 2 and 62% in group 3 retained. Subsequently iron excretion was at approximately normal levels, regardless of duration of hypokinesia with head-down tilt or stimulating substance used. Recovery of hemoglobin mass differed somewhat in the two groups. The authors recommend the ferrocerone test as a technique for evaluating iron reserves before iron deficiency is manifest in the blood.

Table: Types of fractional renal excretion of iron in healthy humans after administration of 300 mg ferrocerone

HEMATOLOGY

Figure: Changes in renal excretion of iron after ferrocerrone loading and hemoglobin mass under conditions of hypokinesia with head-down tilt

PAPERS:

P1212(27/90) Mirrakhimov MM, Kitayev MI, Tokhtabayev AG.
The immune status of individuals suffering from acute altitude sickness.
 Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
 23(6): 62-66; 1990.
 [18 references; 9 in English]

Immunology, Immune Status
 Humans, Males, Individual Differences
 Adaptation, High Altitude Sickness

Abstract: A total of 235 healthy males, aged 18-20, were observed during a 150-day period of adaptation to an altitude of 3600 m above sea level. The subjects were divided into two groups on the basis of adaptive response. Group 1 contained 179 people showing satisfactory adaptation, and group 2 contained 56 men who during the first 3 days of the study developed signs of mild or moderate acute altitude sickness. Diagnosis of altitude sickness was only made if the symptoms persisted for 3 days or more. Immunological examinations were conducted on all subjects at an altitude of 1543 m above sea level. T- and B-cells were identified and measured in lymphocytes extracted from peripheral blood. T-lymphocytes were identified using the method of spontaneous rosette-formation with sheep erythrocytes (E-RFC). B-lymphocytes were identified on the basis of their capacity to form rosettes in response to the erythrocyte antibody complex EAC-RFC. Null (killer) cells were computed by subtraction. Absolute (per 1 ml blood) and relative (in %) levels of E- and EAC-RFC and null-cells were computed. Subpopulations (T_γ and T_μ) of T-lymphocytes were identified through presence on their membranes of Fc-receptors reacting with IgG and IgM. Functional status of the T-lymphocytes was assessed using the blast-transformation response with PHA and concavalin A. B-lymphocyte functioning was evaluated on the basis of level of immunoglobulins in blood serum using the radial immunodiffusion method.

It was found that during the first few days of exposure to high altitudes all subjects displayed a statistically significant decrease in total circulation of E-RFC and blast-transformation response to PHA. Changes were more pronounced in subjects who suffered from high altitude sickness. Normalization occurred on days 25-30 in individuals adapting successfully, but only on day 90 for those who displayed symptoms of high altitude sickness. Absolute concentration of E-RFC was still depressed in the latter subjects after 150 days. T-lymphocyte functioning was also depressed in these individuals, normalizing only after 90 days compared to 25-30 days in successful adapters. Blast transformation response was not depressed at all at high altitudes in successful adapters, but was significantly diminished in those suffering from high altitude sickness. Subjects who developed high altitude sickness had decreased numbers of T_γ cells and elevated numbers of T_μ cells during their initial 3 months at high altitudes. Concentrations of EAC-RFC were depressed in subjects with mountain sickness compared to those adapting successfully. A similar pattern of depression was noted when functional activity of B-cells was measured. Concentrations of null cells were elevated in those with mountain sickness, and differences persisted for 25-30 or 90 days, depending on whether level was considered relative to 1 ml blood, or total amount of circulating blood. It was found that subjects developing mountain sickness had higher baseline levels of null cells, and lower levels of E-RFC and T_μ cells. This may be of significance for selecting individuals likely to adapt well to conditions of high altitude.

Table 1: Concentration of E-RFC in subjects suffering from high altitude sickness during adaptation

Table 2: Blast transformation response with PHA and Con A in patients with high altitude sickness during adaptation

Table 3: Concentration of EAC-RFC in patients with high altitude sickness during adaptation

Figure 1: T γ cells in patients with high altitude sickness and individuals adapting successfully to high altitude conditions

Figure 2: T μ cells in patients with high altitude sickness and individuals adapting successfully to high altitude conditions

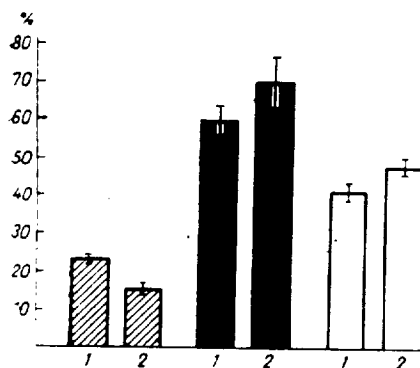


Figure 3: Baseline studies of E-rosette-forming lymphocytes, null lymphocytes and T μ cells (helpers) in patients with high altitude sickness (1) and those adapting successfully (2) to high altitude conditions (3600 m above sea level)

Ordinate - number of cells (in %). Hatched bars - null-lymphocytes; Black bars - E-rosette forming lymphocytes; white bars - T μ -cells (helpers)

P1216(27/90)* Novikov VS, Bortinsovskiy VN.

The effect of smoking on human resistance in a pressurized environment.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 81-85; 1990.

[20 references; 8 in English]

Immunology, Resistance; Cardiovascular and Respiratory Systems; Exercise Tolerance

Humans, Men

Smoking, Habitability and Environment Effects; Pressurized Environment

Abstract: Research was performed on healthy young men spending 2-months in a pressurized environment, performing stressful operator work and undergoing hypokinesia under conditions of only insignificant changes in temperature, humidity, and atmospheric components. The experimental group consisted of 38 smokers, who had smoked for an average of 5 years, and smoked from 10 to 20 cigarettes per day during the experimental period. The control group consisted of 36 nonsmokers. The cellular factor of nonspecific protection, microbial resistance of skin, functional status of the cardiorespiratory system, exercise tolerance, self assessment of state, and incidence of illness were studied. Methods used included determining the absorbing and digestion capacity of leukocytes, skin automicroflora, breath holding on exhalation, vital capacity of the lungs, blood pressure, heart rate at rest and during graded physical activity, written self assessment of health complaints, and symptoms of diseases. Measurements were made 1 month before exposure to experimental conditions and on day 15, and during months 15, 20, and 50 of the experiment. Health complaints and parameters were additionally measured in 240 smokers and 220 nonsmokers working under analogous conditions. Data were tested statistically using Student's t test.

At the beginning (15 days) of their work in the pressurized environment all subjects displayed signs of stress, including increased leukocyte absorbing function and decreased efficiency of intracellular digestion. Effects of experimental conditions were more pronounced in the smokers. After 30 days in the environment, decrease in protective functions was noted, to a more pronounced degree in the smokers. Skin automicroflora levels were higher at all experimental periods in the smokers. On day 60 of treatment, parameters of rate of phagocytosis and effectiveness of intracellular digestion were 16-34% lower in smokers than nonsmokers. Effects on bacteriocidal capacity of lymphocytes were interpreted as due to inhibition of oxygen utilization in smokers. Smokers (52% of the subjects) accounted for 79.5% of the recorded illnesses and had more severe illnesses. Smokers had lower vital capacity of the lungs, higher heart rates, and higher blood pressure, and lower exercise tolerance than nonsmokers. Smokers were more likely to complain of fatigue, bad moods, headaches, and insomnia, as well as having more rapid heartbeat and more frequent angina

Table 1: Parameters of cellular factors of nonspecific protection in smokers working in pressurized environments

Table 2: Parameters of incidence of disease in smokers working in pressurized environments

Figure 1: Automicroflora of the skin in nonsmokers and smokers working in pressurized environments

Figure 2: Level of exercise tolerance in smokers and nonsmokers working in pressurized environments

P1220(27/90)* Ignatova OV, Berlin AA, Pak ZP, Popov IG.

On the protective function of the skin.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 15-19; 1990.

[36 references; 17 in English]

Immunology, Skin, Protective Function

Humans

Operational Medicine

Abstract: This article reviews the literature on the protective function of the skin and how it relates to support of the health of manned space flights. The authors conclude that this function, on one hand, depends on the general resistance of the macroorganism, and on the other, on the composition and biological properties of skin autoflora and is determined as a result of a set of factors: 1) the physico-chemical and biological characteristics of the external environment; 2) the quantitative and qualitative composition of autoflora; 3) the quantitative and qualitative composition of the film of moisture and oils on the skin's surface; 4) the morphological integrity of the epidermis. This must be considered when a system of sanitation and hygiene is developed for spacecraft crews. The third factor, which defines skin type, may be of particular importance for individually tailoring recommendations for selection of cleansing agents for particular crewmembers. Optimal conditions for maintaining the normal functional status of the skin can only be accomplished by considering all of these factors, as well as flight duration.

PAPERS:

P1209(27/90)* Tarasov YuA, Ostovskiy YuM, Satanovskaya VI, Liopo Av, Velichko MG, Abakumov GZ.

Endogenous ethanol in the blood and tissues of rats exposed to hypobaric hypoxia.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 47-51; 1990.

[29 references; 11 in English]

Metabolism, Endogenous Ethanol

Rats

Hypoxia, Hypobaric

Abstract: In this work the authors studied the level of endogenous ethanol in the blood and tissues of 18 white male rats as an indicator of response to hypoxia. Animals were divided into three groups, all of which spent 1 hour in a barochamber. The control group spent the time at normal air pressure of 1020 gPa, experimental group 2 at an altitude equivalent of 2500 m (746.6 gPa), and group 3 at a height equivalent of 5000 m (540.3 gPa). After descent at a rate of 30 m/second, the animals were decapitated and a portion of tissue immediately frozen in liquid nitrogen. Endogenous ethanol was measured using gas-chromatography. Activity of alcohol dehydrogenase was measured spectrophotometrically using ethanol or acetaldehyde as the substrate. The source of enzymes was a supernatant of tissue homogenate first frozen in liquid nitrogen. Activity of NAD-dependent aldehyde dehydrogenase was assessed in the liver and activity of aldehyde dehydrogenase in the bone. Total protein, pyruvate, and lactate and the ratio of lactate to pyruvate were measured in the liver and blood. Antioxidant activity of blood plasma was monitored in the blood and adrenal glands.

Level of endogenous ethanol in blood and tissues turned out to be a sensitive indicator of even short exposure to relatively low levels of hypoxia. This parameter does not seem to be related to the onset of a stress responses, since 11-OCS only increased in animals exposed to the higher hypoxia levels. Parameters of lipid peroxidation likewise increased only in response to the higher level of hypoxia. Changes in levels of ethanol cannot be explained with reference to activity of enzymes metabolizing ethanol, since the latter did not change in a regular fashion. The authors conclude that the concentration of endogenous ethanol in blood and tissues is a more sensitive indicator of exposure to hypoxia than parameters of lactate, lipid peroxidation, or 11-OCS.

Table 1: Activity of ethanol- and acetaldehyde metabolizing enzymes in the liver and brain of rats exposed to varying levels of hypobaric hypoxia

Table 2: The effects of various levels of hypobaric hypoxia on concentration of lactic and pyruvic acid in the liver and blood of rats.

Table 3: Lipid peroxidation in blood plasma in rats exposed to varying levels of hypobaric hypoxia

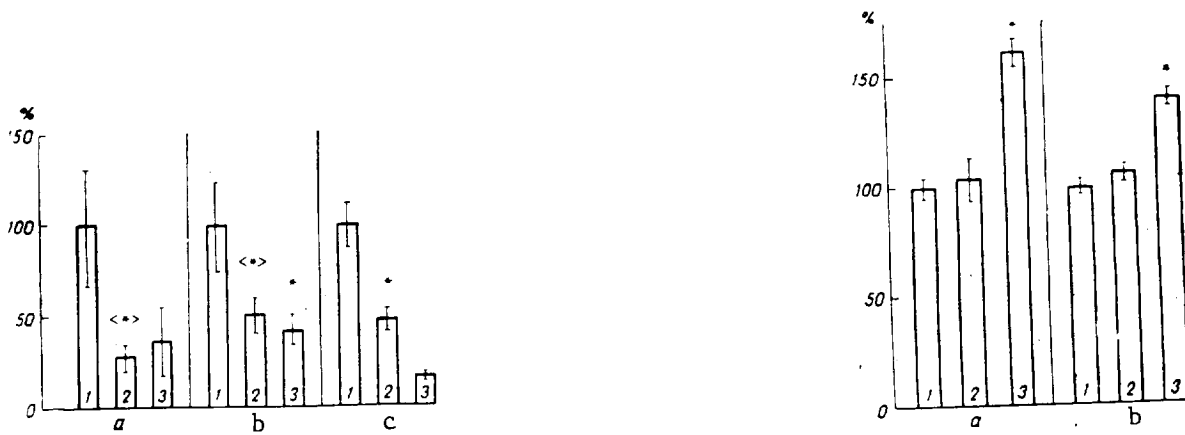


Figure 1: Endogenous ethanol in the liver (a), brain (b) and blood (c) of rats exposed to varying levels of hypobaric hypoxia

Parameters of rats exposed in the barochamber at 765 mm Hg (1) are taken as 100%: 2 - 560 mm Hg (2500 m); 3 - 405 mm Hg (5000 m);
 <*> $p < 0.1 > 0.05$; * $p < 0.05$

Figure 2: Concentration of 11-oxycorticoids in blood (a) and adrenal glands (b) of rats exposed to varying levels of hypoxia. Key: as for Figure 1.

P1217(27/90)* Tolkacheva NV, Levachev MM, Kobozev GV, Safronova LG, Sorokina AG.
Use of the method of thin layer chromatography to study lipid ligands in the serum albumin of athletes.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 85-88; 1989.

[23 references; 2 in English]

Metabolism, Lipid Peroxidation, Serum Ligands

Humans, Athletes

Exercise

Abstract: Studies were performed on human serum albumin obtained using electrophoresis in a polyacrilamide gel. Lipid extracts were obtained with an undescribed method and their concentration measured. Two methods of thin layer chromatography were used to separate out individual lipids. In the first, fractions of free fatty acids were separated with a silica gel in a system of solvents of petroleum ether-ice cold acetic acid (90:10) and stained by spraying on layers of concentrated HCl, with the lipid spots identified using a standard reference spot of ether of free fatty acids and a mixture of standard lipids. The second method was used for studying fractions of phospholipids on plates of the Czech substance "Silufol" in a solvent system consisting of a chloroform-methanol-25% water solution of ammonia (60:35:5); to reveal the fractions, the layers were stained with a solution of rhodamine yellow, and lipids were identified with ultraviolet light. Subject samples were compared with that of a control group. Products of lipid peroxidation were identified by an undescribed method. A group of 22 highly qualified bicyclists, aged 17 to 25, served as subjects in a transitional period of the year's training cycle, during which they were engaging in moderate exercise in team races of 100 km. Blood was taken from the ulnar vein before and after exercise. For comparative purposes blood was studied from 40 normal subjects and 19 subjects suffering from high blood pressure.

The serum albumin of highly trained athletes displayed four additional fractions of phospholipids: phosphatidylethanolamine, sphingomyelin and the minor fraction of phosphatidylinositol, and lysophosphatidylcholine absent in the albumin of the control group. Thus the molecules of this protein were saturated with phospholipids. The rate of the process of diene conjugates and diene ketones increased in the athletes and was associated directly with their level of training. Products of lipid peroxidation decreased in serum albumin as the processes of adaptation to various levels of athletic training progressed. In the pathological state, associated with increased hydroperoxides especially in high blood pressure, such adaptation does not occur.

Table 1: Chemical composition of lipids in serum albumin of subjects

Table 2: Concentration of lipids and products of lipid peroxidation in blood plasma and serum albumin of athletes

P1218(27/90)* Potapov PP.

Activity of NADP-dependent cytoplasmic dehydrogenases in the liver and adipose tissue of rats during recovery after hypokinesia.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 89-90; 1989.

[11 references; none in English]

Metabolism, Cytoplasmic Dehydrogenases, Liver, Fat

Rats

Hypokinesia, Recovery

Abstract: The study of metabolic processes during the period of readaptation after hypokinesia is of interest for its relevance to optimization of countermeasures. This experiment was performed on 75 white rats (60 experimental and 15 controls). Animals' motor activity was limited by placing them in very small individual cages for 30 days. After the experimental period terminated, animals were placed in ordinary group cages. One rat was sacrificed on day 30 of hypokinesia and then one a day for the next 25 days of recovery. Data was processed using the moving average method. Significance of differences was tested using the Wilcoxon Mann Whitney non-parametric test. In the first experiment, activity of isocitrate dehydrogenase (ICDH) and glucose-6-phosphate dehydrogenase (G-6-PDH) were measured in the liver and adipose tissue. In the second experiment, activity of NADP-dependent malate dehydrogenase (MDH) was measured in the liver. The cytoplasmic fraction was isolated in a refrigerated chamber at a temperature of 0-4°C.

On day 30, activity of G-6-PDH was elevated by 33% in the liver compared to control animals. During the initial portion of the recovery period, activity of ICDH and G-6-PDH was statistically significantly elevated in liver and adipose tissue compared both to control levels and levels during hypokinesia. Activity of liver G-6-PDH remained elevated until day 19 of recovery, and dropped below normal on days 21-23. ICDH activity in the liver normalized at the end of the first week of recovery, dropped below normal on days 9-18, and subsequently normalized. Activity of MDH was depressed during the first week of readaptation and elevated from days 10 to 19. In adipose tissue, activity of G-6-PDH continued to be elevated until day 17 and that of ICDH only until day 6. Activation of ICDH and G-6-PDH in the liver during the early adaptation period may be considered an appropriate metabolic reaction providing increased production of NADPH, while depressed activity of cytoplasmic ICDH between days 9 and 18 of recovery may be associated with consumption of ICDH on other metabolic paths. Decreased activity of NADP-dependent MDH during early readaptation may be associated with increased gluconeogenesis. It should be borne in mind that activity of ICDH is significantly higher than activity of G-6-PDH and MDH, thus potential production of NADPH in the liver is only elevated during the early period after removal of animals from hypokinesia. During readaptation animals' need for reducing synthesis is elevated. After hypokinesia this might lead to a relative deficit in NADPH, which should be considered an adverse change in metabolism.

Figure 1: Changes in activity of cytoplasmic NADP-dependent dehydrogenases in the liver in rats during readaptation after hypokinesia

Figure 2: Changes in activity of cytoplasmic NADP-dependent dehydrogenases in fatty tissue in rats during readaptation after hypokinesia

MUSCULOSKELETAL SYSTEM

P1206(27/90)* Belakovskiy MS, Khaidakov MS.

Effects of active metabolites of Vitamin D₃ on the bones of rats exposed to different hypokinesia paradigms.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 36-39; 1989.

[18 references; 11 in English]

Musculoskeletal System, Bones; Metabolism, Calcium, Phosphorus

Rats, Male

Nutrition, Vitamin D₃ Metabolites, Hypokinesia, Tail Suspension, Immobilization Cages

Abstract: Previous experiments have shown that active metabolites of vitamin D₃ help to optimize calcium-phosphorus metabolism and the state of bone tissue in hypokinesia created using immobilization cages. The current experiment compared these effects to those obtained using the tail suspension paradigm. Subjects were male Wistar line rats. The animals received a semisynthetic diet with a 0.6% concentration of calcium and phosphorus. Hypokinesia was created either through immobilization cages or tail suspension for a period of 6 weeks. Some of the animals received oral doses of 1,25(OH)₂ and/or 24,25(OH)₂D₃ in doses of 0.025 and 1.25 mg/day. After treatment, the animals were sacrificed and measurements made of total calcium, inorganic phosphate, and PTH in blood serum; and volume, density, and levels of calcium, phosphorus in mineralisates of epiphyses and central areas of the diaphyses of the femur bones. Active transport of calcium in the small intestine was assessed on the basis of differences in absorption of ⁴⁵Ca by disks from the duodenum when incubated in a medium perfused with carbon or nitrogen.

Tail suspension was associated with some inhibition of rate of weight increase and a moderate but insignificant increase in PTH and some increase in absorption of calcium in the intestine. The distal epiphyses of the femur in these animals displayed a slight decrease in volume, and a sharp decrease in density and calcium and phosphorus levels; while the central regions of the diaphysis displayed an increase in density and mineral levels. Maintenance in the immobilization cages was associated with a reliable decrease in body weight and the development of hypocalcemia with PTH unchanged and calcium absorption in the intestine diminished. The volume of the epiphyses decreased substantially. The proximal epiphyses displayed both a decrease in density and concentration of minerals, while in the distal epiphyses these parameters remained at control level. Changes in the diaphyses were analogous to those occurring in the tail-suspension paradigm.

Oral administration of active metabolites did not lead to changes in body weight, either alone or in combination. In suspended animals receiving metabolites, no changes were noted in blood calcium or phosphorus, or rate of accumulation of calcium in the intestine. PTH decreased when either or especially both metabolites were administered. Animals of all groups responded to the metabolites with marked increase in density and volume concentration of calcium and phosphorus in the distal epiphysis and diaphyses.

Combined administration of D₃ metabolites to animals immobilized in cages led to normalization of total calcium in blood and some increase in rate of accumulation of calcium in the intestine. There was a significant increase in density and mineral levels in the proximal epiphyses, while there were virtually no changes in the distal epiphyses or diaphyses. The authors conclude that bone changes resulting from hypokinesia are mainly produced by local factors that increase bone sensitivity to systemic influences.

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Table 1: Effects of $1,25(\text{OH})_2\text{D}_3$ and $24,25(\text{OH})_2\text{D}_3$ on increase in body weight, concentration of calcium, phosphorus, and PTH in blood serum and absorption of ^{45}Ca by the mucous membrane of the small intestine of rats exposed to different experimental hypokinesia paradigms

Table 2: Effects of $1,25(\text{OH})_2\text{D}_3$ and $24,25(\text{OH})_2\text{D}_3$ on volume, density and levels of calcium and phosphorus in the epiphyses of rats exposed to different experimental paradigms of hypokinesia

Table 3: Effects of $1,25(\text{OH})_2\text{D}_3$ and $24,25(\text{OH})_2\text{D}_3$ on length, density and levels of calcium and phosphorus in the diaphyses of rats exposed to different experimental paradigms of hypokinesia

MUSCULOSKELETAL SYSTEM

P1207(27/90)* Shvets VN, Pankova AS, Gol'dovskaya MD. Vnukova ZE.

Changes induced by hydroxydimethyl aminopropylidene diphosphonate in the response of bone tissue in rats to hypokinesia.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 39-42; 1989.

[14 references; 10 in English]

Musculoskeletal System, Bone Tissue; Metabolism, Calcium

Rats, Male

Hypokinesia, Immobilization Cages, Hydroxymethyl Aminopropylidene Diphosphonate

Abstract: Hydroxydimethyl aminopropylidene diphosphonate (Russian abbreviation: AMOK) has been suggested as an agent to modify disorders of calcium metabolism. This study investigated its effects on bone changes associated with hypokinesia in a total of 180 male Wistar rats. In experiment 1, subjects were injected subcutaneously with 5 mg/kg AMOK for a period of 10 days, after which 10 were sacrificed and their bones used as a baseline control. The remaining rats were divided into 2 equal groups. One group was housed in immobilization cages. The others were maintained under ordinary vivarium conditions. On days 7, 15, and 35 10 rats from both groups were sacrificed. In experiment 2, animals were housed in immobilization cages. One group was injected daily with 0.01 mg/kg AMOK. The other group served as a control. On days 7, 15, and 35 10 rats from each group were sacrificed. An intact group of 40 rats served as an additional control. All animals ate the same diet. The tibia bone and lumbar vertebra were isolated from each rat sacrificed. Material was fixed, decalcified, and embedded in paraffin. Histological sections 5-7 μ m thick were made laterally through the center of the bone, and stained.

Using an ocular test system, measurements were made of volume density of spongy bone in the proximal area of the metaphysis of the tibia and throughout the body of the vertebra. Volume density of spongy bone was measured at a magnification of 280 X in the zone of the primary spongiosa throughout its length. Volume density of bone was computed according to the formula: $V = (N/289) \cdot 100\%$, where V is volume density and N is the number of points in the structure of the trabeculae. Student's t was used to test data for significance.

Volume density of spongy bone decreased as early as day 7 of hypokinesia, and then remained at this new lower level. In week 1 decrease in bone mass was associated with the stress response, while failure of the loss to continue was due to adaptation of bone tissue to hypokinesia. Where AMOK in a dose of 0.01 mg/kg was injected daily starting at the start of hypokinesia, then the reaction of bone tissue was completely prevented and, indeed weight of spongy bone even began to exceed baseline. This was due to inhibition of resorption and growth in bone length. When injection of AMOK for 10 days preceded hypokinesia, bone mass increased substantially compared to control. When animals with increased bone mass were then subjected to hypokinesia, the response was similar to that of "pure" hypokinesia, confirming that initial loss was due to stress. However, after the first week of hypokinesia, bone mass recovered to baseline in the animals treated with AMOK. Animals treated with AMOK and maintained under normal conditions continued to show elevated bone mass. Thus, AMOK did not prevent the stress response of bone, but did interfere with "adaptive" decrease in its mass.

MUSCULOSKELETAL SYSTEM

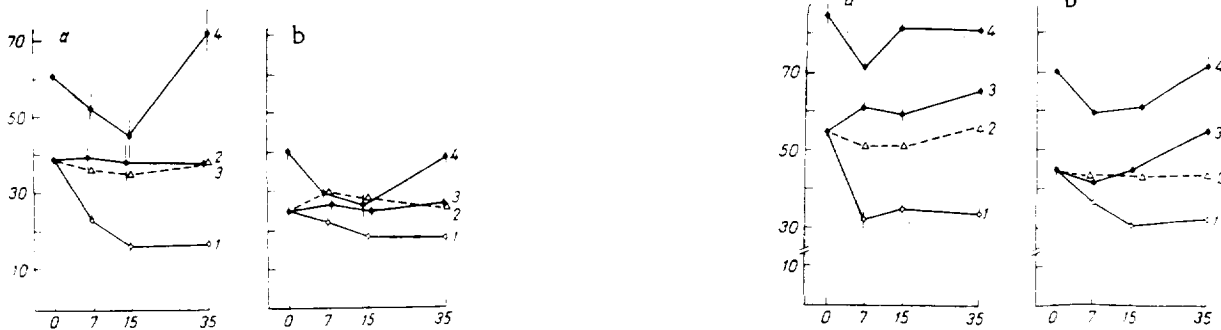


Figure 1 Volume density of all spongy bone in the metaphysis of the tibia bone (a) and body of the vertebra (b)

Here and in Figure 2: 1 - "pure hypokinesia"; 2 - intact control; 3 - AMOK injected during hypokinesia in a dose of 0.01 mg/kg; 4 - AMOK, injected 10 days before hypokinesia in a dose of 5 mg/kg. Abscissa - day of the experiment; ordinate - absolute value of volume density of bone (in %)

Figure 2: Volume density of spongy bone localized in the primary spongiosa of the tibia (a) and vertebra body (b)

MUSCULOSKELETAL SYSTEM

P1222(27/90) Stupakov GP, Volozhin AI.

Changes in human bone under conditions of bedrest and weightlessness: The human skeleton under conditions of bedrest and weightlessness.

136 - 147

In: M157(26/90) Stupakov GP, Volozhin AI.

Kostnaya Sistema i Nevesomost'; Костная Система и Невесомость

[The Skeletal System and Weightlessness].

Volume 63 In series: Problemy Kosmicheskoy Biologii,
Leningrad: Nauka; 1989.

Musculoskeletal System, Bone; Mechanical Properties; Bone Minerals
Humans, Cosmonauts, Patients, Osteoporosis
Space Flight, Salyut-6, Bedrest

Abstract: This section deals with results of studies of the mechanical properties of the human vertebra and the rate of development of osteoporosis in real and simulated microgravity using parameters that enabled the quantitative assessment of changes. One study utilized autopsied material from patients who had died after 20-40 days of bedrest and also subjects in bedrest experiments and cosmonauts on Salyut-6.

Autopsied material was used to study the mechanical properties of human bone vertebrae and parameters of their physical/chemical properties. In the bedrest experiment and in cosmonauts the density of the structure of the head bone was studied using direct photon absorptiometry.

The sternal and lumbar vertebrae (T₁₀-L₃) were isolated from 9 corpses of individuals, aged 22 to 46. Of these 5 had undergone therapeutic bedrest 20 to 42 days in duration before dying of sudden complications, such as myocardial infarction. Control material came from the vertebrae of 4 individuals who had died of accidents and had not been restricted in motor activity. Bone material was isolated no later than 24 hours after death, and each vertebra was carefully stripped of soft tissue. The mechanical testing of the vertebrae for compression strength utilized a standard machine with rate of loading of 10 mm/min. In addition to mechanical properties, mineral saturation of the vertebrae and the elements contained in its mineral components were determined.

It was discovered that the vertebrae of individuals who had undergone bedrest displayed diminished resistance to destruction and deformation, as indicated by decreased bearing capacity, rigidity, and energy of elastic deformation. In people who had died of accidents the bearing capacity of the vertebrae was a direct function of the amount of mineral substance in them. In those undergoing bedrest, this relationship still held, although for a given quantity of minerals vertebra strength was lower than in the normal activity groups. There was no difference between the mineral contents of the vertebrae of both groups. In the group that had engaged in normal activity before death, maximum strength, specific energy, and modulus of elasticity were 68.9, 1.48, and 1700.2, kgf/cm², respectively. Corresponding values for the bedrest group were 47.1, 1.01, and 1169.4 kgf/cm². These differences were highly significant. Only the parameters of relative deformation were the same in both groups.

When the mineral composition of bone was studied, it was found that bones of the bedrest subjects had diminished concentrations of Ca, but retained normal P and Mg with Na and particularly K elevated. The possibility that altered mineral composition had affected vertebrae strength was tested through derivation of multiple linear regressions. In normal subjects dying in accidents, the highest association was between ultimate strength of the vertebrae and mineral saturation ($r=0.739$). In the bedrest group this correlation was diminished ($r=0.302$).

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Multiple regression with concentrations of Ca, P, and Mg was considerably higher ($r=0.779$) for the bedrest group (control group $r=0.886$). The authors interpret this as indicating that decreased vertebra strength in the bedrest group can be attributed largely to altered mineral composition (particularly the decrease in Ca) of bone substance. Addition of Na and K to the multiple regression increased r only slightly.

The authors hypothesize that during the early stage of unloading, corresponding to the activation of resorption processes, there is a partial restructuring of bone tissue involving the formation of defective crystals of hydroxyapatite, or else the loss of Ca ions from the crystal surface occurs independently of restructuring. In either case the strong ionic and hydrogen bonds between organic and mineral components are weakened, in turn weakening the stiffness of collagen, and increasing deformability of bone substance and decreasing its strength.

The authors argue that the phase of decreased bone strength without loss of mass is transient in nature, and thus of limited practical significance compared to loss of strength due to osteoporosis. However, this stage may be of significance for short-term (approximately 1 month) space flights.

Loss of bone mass and thus associated mineral component occurring in osteoporosis result in negative calcium and phosphorus balance. Thus quantitative analyses of bone density and mineral balance should be performed to assess rate and severity of structural skeletal changes in real and simulated weightlessness. Decreased bone density has been observed through photodensitometry in cosmonauts and astronauts after relatively short space flights. However, results suggesting that up to 20% of minerals are lost from certain bones turned out to be inflated due to an error inherent in the measurement technique.

The method of direct photon absorptiometry enabled more accurate determination of the extent of bone demineralization occurring in space. The authors summarize American data from flights of Skylab, Gemini-7, Apollo-7 and 11, as well as Western hypokinesia data. The conclusion they draw from this work is that relatively slight values of negative Ca balance may be associated with substantial loss of mass of spongy bone, indicating inhomogeneity of development of osteodystrophy in various areas of the skeleton. They emphasize the importance of individual differences in such processes. In their own research they have noted that density of structural composition, as estimated from mineral saturation, varies in healthy individuals aged 20-25 within broad limits from 0.135 to 320 g/cm³. Individuals with high initial bone mineral saturation may suffer loss of bone mass that would not be revealed using x-ray techniques.

The authors studied the effects of 30 and 120 days of experimental bedrest on concentration of minerals in the heel bone, using direct photon absorptiometry (Bone-Scanner-7102 instrument). In the 30-day condition, subjects were examined twice, on the days before and after treatment. In the 120-day conditions mineral levels were measured several times during treatment and used to compute bone atrophy in percentage terms as a function of time, using regression analysis for each subject. This method enabled a more accurate measurement of mean monthly loss of mineral substance. Results, in the table below, suggest that mean monthly bone changes were higher for the 30-day condition than the 120-day one. Subjects in the former were younger and the difference may be due to their faster metabolic rate.

A study of Salyut-6 cosmonauts included individuals exposed to space for 140, 175, 184 and 75 days. Examinations were made 1 month preflight, with the exception of crewmembers for the 140-day flight. For these two cosmonauts baseline data were measured 1.5 and 2 years preflight. Postflight examinations were performed 2-4 days after landing. The results are presented in the table below. On the whole, the mean monthly extent of bone atrophy in cosmonauts was lower than in the bedrest studies for subjects with equivalent metabolic rates.

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This lower rate of dystrophy may be associated with the use of prophylactic measures on board the station.

It should be noted that in crewmembers participating in two flights (captain of the first and fourth, flight engineer of the second and third), the mean monthly parameters of bone atrophy were very close for both cases, although the former estimated he had devoted more work to prophylactic measures on his second flight. This may show the leading role played by individual differences in rate of development of osteoporosis during exposure to space.

Table 21: Changes in mechanical properties of bones in humans after 20-40 day periods of bedrest

Table 22: Multiple regression analysis of the ultimate strength of vertebrae, their mineral saturation and mineral composition

Table 23: Results of experiment (Hansson et al.,1975)

Table 24: Results of examinations of subjects undergoing 30- and 120-day period of bedrest

Bedrest duration, days	Subject	Age,yrs	Weight, kg	Height, cm	Metabolism cal/kg/day	Heel bone atrophy,%	
30	1	20	68.5	170	25.20	6.49	
	2	22	67.5	178	25.75	2.39	
	3	20	63.6	171	26.15	7.11	
	4	20	75.0	180	24.88	1.1	
	5	20	63.0	165	25.79	3.91	
	6	20	67.0	165	25.07	9.3	
Mean		20.3	67.4	171.5	25.47	5.05	
Bedrest duration, days	Subject	Age,yrs	Weight, kg	Height, cm	Metabolism cal/kg.day	Heel bone atrophy,%	
120	1	30	75.3	181	23.8	Total 15.6	Monthly 3.9
	2	44	89.8	172	20.8	12.2	3.05
	3	32	80.8	173	22.6	3.98	1.0
	4	36	84.0	177	22.2	13.9	3.5
	5	35	68.6	164	23.3	17.2	4.3
	6	30	91.5	176	22.0	21.7	5.4
Mean		34.5	81.7	173.8	22.45	3.53	

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Table 25: Results of examination of Salyut-6 crewmembers

Crew	Flight duration	Cosmonaut	Age, yr	Weight, kg	Height, cm	Metabolism cal/kg/day	Heel bone dystrophy. % total mean monthly
1	140	Captain	36	84	172	20.88	3.0 0.65
		Engineer	38	76	177	24.93	19.8 4.3
2	175	Captain	38	79	169	22.41	9.8 1.7
		Engineer	39	84	182	21.58	3.0 0.52
3	184	Captain	35	71	172	24.72	9.6 1.59
		Engineer	40	85	182	21.33	4.4 0.73
4	75	Captain	39	83	172	20.67	0.9 0.37
		Engineer	41	72	175	21.0	3.2 1.3
Mean			38.3	79.3	175.1	22.19	1.40

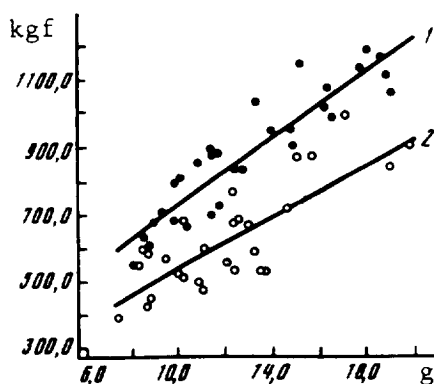


Figure 39: Carrying capacity of vertebrae as a function of mass of mineral substances they contain

- 1 - normal motor activity, 2 - after 20-40 days of bedrest
 1 - $y = 221.790 + 51.006x$, $p < 0.01$, $r = 0.879$;
 2 - $y_2 = 153.465 + 38.614x$, $p < 0.01$, $r = 0.767$

MUSCULOSKELETAL SYSTEM

P1223(27/90) Stupakov GP, Volozhin AI.

Changes in human bone under conditions of bedrest and weightlessness: Bone changes when functional loading of the skeleton is reduced from the standpoint of rapid and slow-developing osteoporosis.

147-150.

In: M157(26/90) Stupakov GP, Volozhin AI.

Kostnaya Sistema i Nevesomost'; Костная Система и Невесомость

[The Skeletal System and Weightlessness].

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Leningrad: Nauka; 1989.

Musculoskeletal System, Bone

Humans

Reduced Functional Loading, Osteoporosis, Rapid and SlowDeveloping

Abstract: Rate of development of osteoporosis may vary considerably in different functional and pathological states. The typical example of slow-developing osteoporosis, involutional or physiological osteoporosis, involves slow, generally equal losses of bone mass from the spongy and compact structures of both the peripheral and central skeleton. In rapid-developing osteoporosis, due to various metabolic shifts, loss of bone mass begins in the center of the body and only later spreads to the periphery. The earliest and swiftest changes occur in the vertebrae, then in the bones of the pelvis and long bones, and significantly later in the compact bones, when loss of mass in the spine has already ceased. Bone loss in real and simulated weightlessness should be classified as rapidly developing. However, the biophysical and biomechanical properties of human bone have only been studied in slow-developing osteoporosis, although the changes in the skeleton associated with involutional processes on the one hand and decreased functional loading of bones on the other appear identical. In the latter case more profound structural changes are likely, accompanied by drastic decrease in strength. For this reason changes in bone strength in old age evidently cannot be considered a complete analog of changes due to disuse.

MUSCULOSKELETAL SYSTEM

P1224(27/90) Stupakov GP, Volozhin AI.

Changes in human bone under conditions of bedrest and weightlessness: General principles of bone changes under conditions of weightlessness and its simulations.

150- 158.

In: M157(26/90) Stupakov GP, Volozhin AI.

Kostnaya Sistema i Nevesomost'; Костная Система и Невесомость

[The Skeletal System and Weightlessness].

Volume 63 In series: Problemy Kosmicheskoy Biologii,

Leningrad: Nauka; 1989.

Musculoskeletal System, Bone; Metabolism, Metabolic Rate, Calcium

Humans, Rats, Dogs

Weightlessness, Simulated Weightlessness

Abstract: The variability in increase in negative calcium balance in response to unloading of the weight-bearing system in cosmonauts and experimental subjects has been shown to relate to two factors: initial density of bone structures and rate of metabolic processes, both general and local that determine the activity of processes of physiological restructuring of bone. Two methods may be used to determine the rate of resorption of various bone structures in humans: one based on an intraspecies model of bone atrophy and the other based on an interspecies model.

To develop the intraspecies model, a quantitative evaluation must be performed of the extent of negative calcium balance as a function of time, serving as an equivalent to loss of bone mass. To do this, American data on calcium balance were used from 85 subjects spending varying amounts of time in strict bedrest and from 9 astronauts completing 28- to 84-day Skylab flights. By integrating data in the literature concerning calcium balance over time, a function relating total calcium loss to duration of bedrest or space flight was constructed (Figure 40). This figure shows that loss of calcium varies broadly from individual to individual, although its level in space flight lies virtually within the error bar for bedrest. This allows bedrest to be considered a completely adequate model of weightlessness with respect to the bone system.

Loss of calcium of up to 40 g for 9 months of bedrest amounts to approximately 4% of its total level in the skeleton. Loss of this magnitude does not present a threat if it reflects homogeneous resorption of bone substance throughout the entire skeleton, but could become dangerous if it progressed.

Rats develop osteoporosis of the epiphysis of the femur in weightlessness (distal epiphysis, head), i.e., in areas of spongy substance. Loss of bone mass estimated on the basis of mineral saturation reached 18-21% without any signs of osteoporosis in the compact substance of the diaphysis. Analogously, when dogs were placed in conditions where the supporting function of the hind legs was eliminated for 3 months, atrophy of the spongy structures in the distal epiphysis reached an average of 33% and had virtually reached a plateau, while in the diaphysis only the initial signs of osteoporosis could be seen. This corroborates data in the literature attesting to the fact that in rapidly developing osteoporosis in humans, atrophic changes in compact bone occur significantly after stabilization of atrophy of spongy bone.

Non-weight-bearing bones, even in their spongy component, do not undergo osteoporosis during space flight or bedrest. Thus, there is basis for a hypothesis that the negative calcium balance occurring with elimination of weight loading relatively early is due mainly to resorption of spongy bone of the axial skeletal. Rate of resorption may differ for various portions of the skeleton, as will rate of physiological restructuring of one or another structure.

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Presuming the interrelationship of these processes, the authors developed a methodology for evaluating the severity of atrophy in the spongy structures of the axial skeleton, which took into account data on the mass of spongy substance, concentration of calcium and rate of physiological restructuring. For this the authors used material cited by experts in the International Commission on Radiation Protection and V. Schneider's results of research on calcium balance in 90 subjects undergoing strict bedrest, 12 for 20 weeks. Mean loss of calcium during this time was 23 g. Two assumptions were made when using this data. First, because of absence of information on the quantity of spongy substance separately for the distal and proximal epimetiphysary areas of the femur bones, they were assumed to be equal. Second, the mean parameter for renewal of analogous structures of the femur bone was taken as the rate of renewal of spongy tissue in the tibia and foot bones. Results of the analysis are given in Table 26. In addition, the authors directly evaluated total calcium in the bodies of vertebrae T1-L5 in three men with average anthropometric parameters. Good agreement with the data in the table was achieved.

It is completely justified to use the amount of calcium loss from specific bones as a measure of bone atrophy, since the rat and dog experiments described above showed that the extent of mineralization of bone substance (ash content, %) and its ratio of Ca:P, changes insignificantly if at all and here can be ignored.

Computation of rate of atrophy of bone tissue (v_{x1}) in general is described by the following equation: :

$$v_{xi} = m_4 \cdot v_i / \Sigma m_{3i}, \text{ where } \Sigma m_{3i} = \Sigma m_{1i} \cdot v \cdot a / 10^4.$$

where i - is the bone index, m_4 is the total loss of calcium for the period studied, in g; v_i is the rate of physiological restructuring, in % per year. Σm_{3i} is the total mass of renewed calcium in g/year, m_i is the mass of spongy bone, g, and a is the concentration of calcium in it in %.

This estimate of rate of atrophy for bones of the pelvis and foot agree well with data on direct or instrument based evaluations of the rate of thinning of structures of the iliac and heel bones. Thus, based on study of 34 bone fragments taken from the iliac of patients undergoing strict bedrest, atrophy averaged 6%, and in the heel bone at various times of the experiment in various numbers of subjects fluctuated between 0 and 8.4%, averaging 4% per month. Data from studies of the vertebrae of patients undergoing long-term bedrest were close to computed rate of atrophy for the vertebral column.

Available data on extent of bone atrophy in the vertebral column obtained by a new method of computer tomography, are contradictory. Some data show rate of resorption of bone substance in the vertebrae exceeding by a factor of 5 the corresponding parameter for spongy structures of the peripheral skeleton, while other data assess these parameters as relatively close. Data obtained from the authors' calculations puts the ratio at approximately 2:1.

It may be demonstrated graphically that rate of atrophy of various structures during the period of active development of osteoporosis is a function of total loss of calcium by the body. As Figure 41 shows, experimental and computed parameters on extent of atrophy of structures of the heel bone as a function of total loss of calcium by the body correspond. This graph can be used as a nomogram to determine loss of bone mass as a function of magnitude of negative calcium balance. To do this one also needs to measure concentration of calcium in the vertebral column. Based on data from Figure 41, one may retrospectively assess the results of work to identify X-ray indicators of osteoporosis in the iliac bone and proximal epiphysis of the femur. Osteoporosis was diagnosed for loss of calcium from 15 to 36 g, which according to the function cited corresponds to bone atrophy in the areas studied of approximately 18-40% (for mean initial density of the bone structure). Evidently this level of bone atrophy in the area studied may be diagnosed using X-rays, since the total thickness of the trabecular structures is small here.

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Thus there is good agreement between the measured and derived extents of loss of bone mass in the heel and iliac bones, proximal metaphysis of the femur and vertebral column. The data in this model show that the most rapid resorption occurs in the vertebral column, which, moreover, contains the major portion of spongy substance of the whole axial skeleton. Thus, the negative calcium balance is due largely to atrophic changes in the vertebral column. It is no accident that, in 30 subjects studied during 60-day periods of bedrest in which they were permitted to sit up, not a single instance of negative calcium balance was found. Taking into account that the processes of atrophy of spongy structures ceases relatively early, after less than a year, negative calcium balance persisting after that period is evidently associated with the development of processes of resorption of compact substances.

Before ending the consideration of the intraspecies model, it should be noted that the conditions of weight unloading that occurs during bedrest are not the same for all areas of the axial skeleton, since passive muscle tonus does not increase the level of purely internal stress in the vertebral column, characteristic of other bones of the skeleton. This circumstance is an additional reason to also consider interspecies models of bone atrophy.

The interspecies model entails consideration of two principles which the authors have established: the relative rate of atrophy of bone tissue is an inverse function of the initial concentration of mineral substances in spongy bone, and the extent of osteoporosis is directly proportional to the rate of basal metabolism, which follows from interspecies functions.

Before considering the model, it would be useful to consider interspecies characteristics of the state of the mineral phase of bone, since it may be associated with rate of physiological restructuring and at the same time determine the mechanical properties of bone. Existing data attest to interspecies differences in parameters of mineral saturation of the bone structures studied, with smaller differences in the extent of mineralization and concentration of the basic elements composing hydroxyapatite: Ca and P.

It should be noted that the extent of mineralization and the quantitative characteristics of mineral composition are accounted for in the integral parameters of mineral saturation, which also reflect compactness of composition of trabecular structures. It is no accident that the dynamic strength of the vertebra Y_1 in humans (studied by subjecting segments T_{11} - L_3 to triangular impact of 50-70 msec in duration), the static strength of vertebra Y_2 , and also the static strength of spongy structures in dogs (distal epimetaphysis zone of the femur, Y_3) and in rats (head of the femur bone, Y_4) are closely related to their mineral saturation. The association between these values can be described by equations of the exponential or parametric types:

$$Y_1 = 1(0.0696 - 0.399x_1 + 0.64x_2^2) \quad r=0.912$$

$$Y_2 = 16.7 \cdot 1022.7^x, \quad r=0.884$$

$$Y_3 = 1110.8x^{1.99} \quad r=0.933$$

$$Y_4 = 52.36 \cdot 58.88^x \quad r=0.982$$

where x - mineral saturation in g/cm^3 , x_1 and x_2 are bodies T_{10} and T_{11} of the vertebra, respectively, and x_3 and x_4 are the corresponding areas of the femur bones of dogs and rats. Strength parameters (Y) for these equation are expressed in kgf/cm^2 .

Figure 42 shows the general function relating the mechanical properties of bone to mineral saturation. Not only do these functions correspond to parameters of normal and osteoporotic bone, they appear to be universal for different species. This fact is highly consistent with data on the mineral phase of bone. It also may be that the level of mineral saturation itself is a

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function of rate of physiological restructuring of bone tissue, which also follows from the equation presented in Table 25.

Construction of the interspecies model involved creation of an index reflecting the ratio of basal metabolism to mineral saturation, since these two parameters have opposite effects on rate of atrophic changes. In rats, mineral saturation of the distal epiphysis and the head of the femur, and also rate of resorption of bone were approximately the same, allowing the mean parameters (0.600 g/cm^3 and 17.8% per month) to be utilized in the ratio. In dogs, mineral saturation of the bone in the distal epimetaphysial zone was 0.253 g/cm^3 with a rate of atrophy of 11% per month, while the corresponding values for the head of the femur were 0.372 g/cm^3 and 6.2% . Thus ratios for the dog were computed separately. Resulting functions of rats, dogs, and humans are linear in nature (Figure 42). Human data on atrophy rate of the heel bone were obtained from a 20-week bedrest experiment performed by Schneider. Using the derived function and the estimate that mineral saturation of the human vertebrae is 0.226 g/cm^3 , the index is equal to 113.6 and the predicted atrophy rate is an average of 7.3% per month. Individual data on metabolic rate and mineral saturation of bones can be used to predict individual rates of dystrophic processes.

The prediction function was tested for the heel bone of 6 healthy young subjects spending 1 month in strict bedrest. Results of the prediction were virtually identical to data from instrument-based measurement of the heel bone. Mean-monthly development of osteoporosis in the heel of cosmonauts was well predicted by the model. However, this was not the case for the vertebrae. American data (Cann, 1982) show loss of mineral substances from the vertebrae of approximately $1/4$ of the predicted value. The authors attempt to explain this discrepancy with reference to osmotic pressure and increased hydration of the disks. It would be expected that subjects in whom hydration is abnormally low would show osteoporosis of the vertebrae close to that predicted.

Table 26: Data on rate of dystrophic changes in the spongy structures of the axial skeleton in response to decreased weight loading

Bone	Spongy bone, g	Ca, g	Restruct, %/yr	g Ca renewed/yr	% Ca renewed/yr	% Ca lost in 20 wks	Atrophy in 20 wks, %	Bone atrophy %/month
Vertebral column	330	3.8	8.3	3.15	55.2	12.7	33.5	7.3
Pelvis bones:	40	4.6	6.5	0.30	5.2	1.2	26.1	5.7
Femur								
proximal	130	1.5	5.7	0.85	15.0	3.4	23.0	5.0
distal	130	1.5	2.5	0.37	6.5	1.5	10.0	2.2
Sacrum	25	2.9	6.5	0.19	3.3	0.71	26.6	5.8
tibia	160	18.4	4.1	0.75	13.2	3.13	16.4	3.6
fibula	5	0.6	4.1	0.02	0.4	0.095	16.2	3.5
Foot bones	15	1.7	4.1	0.07	1.2	0.283	16.9	3.7

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Table 27: Parameters of the mineral phase of spongy bone

Subject	Bone	Mineral density, g/cm ³	Ash content%	Concentration of elements per 100 g ash			
				Ca, g	P, g	Na, mg	K, mg
Humans	Body of vertebra	0.218	46.0	42.70	14.30	601.0	64.2
Dogs	Distal epimeta-physis of femur	0.253	59.48	41.13	14.68	516.0	44.9
Rats	Head of femur	0.600	60.0	43.5	17.2	380.0	40.0

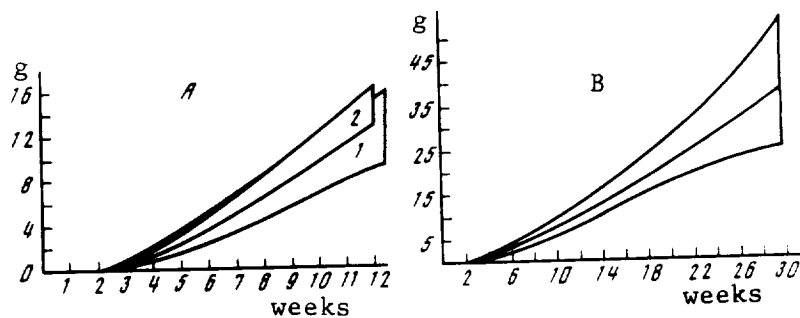


Figure 40: Loss of calcium as a function of time. A - in equal periods of bedrest (1) and spaceflight (2), B - in bedrest of up to 30 weeks.

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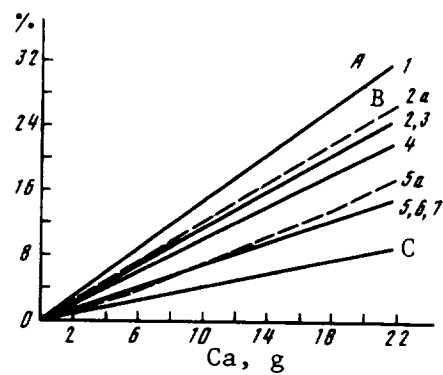


Figure 41: Extent of atrophy of spongy structures of the axial skeleton as a function of loss of organic calcium

A- computed results, B - research data: vertebral column; 2, 3 - bones of the pelvis, sacrum; 4 - proximal epiphysis of the femur; 5, 6, 7 - tibia, fibular, foot bones; 8 - distal epiphysis of the femur; 2a = iliac (Minaire, 1974); 5a - heel bone (Donaldson et al., 1970; Schneider, 1977).

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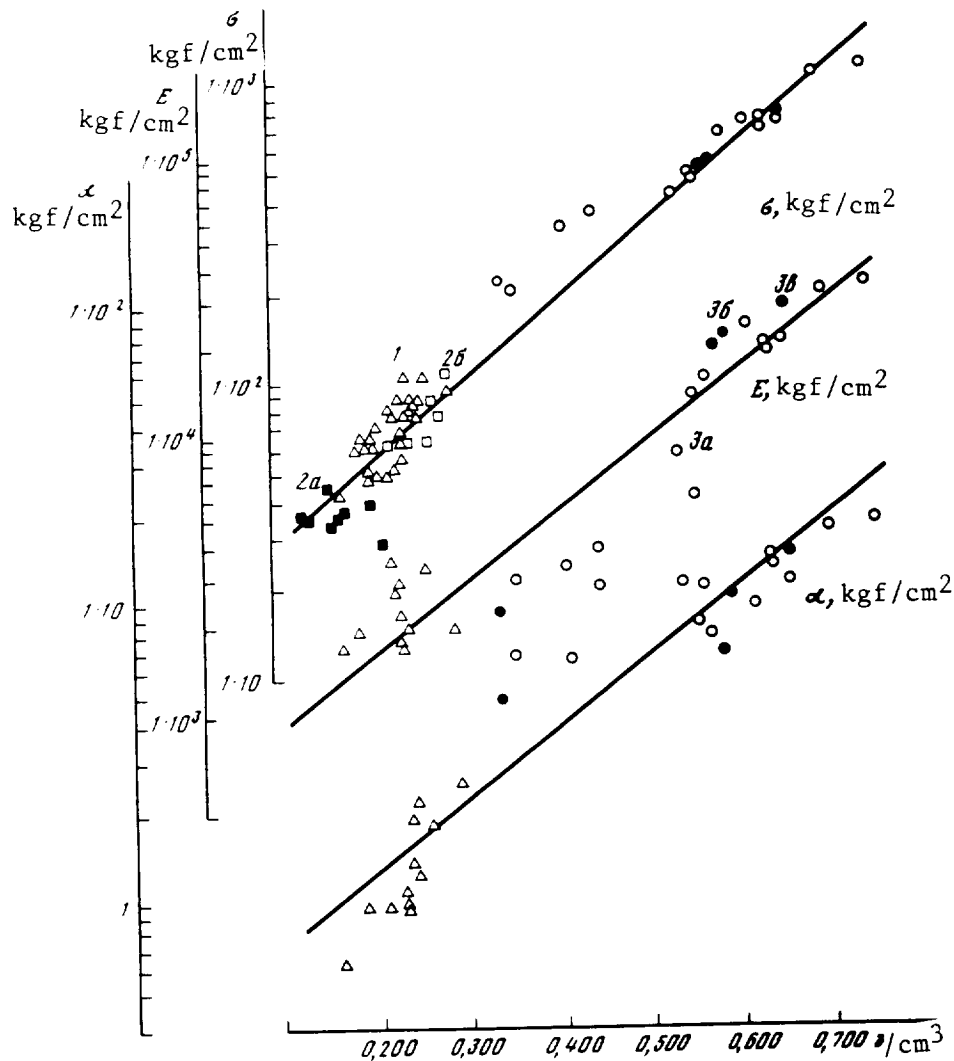


Figure 42: Mechanical properties of spongy bone structures as a function of their mineral saturation

1 - human spine; 2a - distal epimetaphysis of the femur in control dogs; 2b - with osteoporosis; 3a - head of the femur of control rats (mean group data); 3b - in osteoporosis; 3c - after readaptation period. Ordinate - ultimate strength (σ), modulus of elasticity (E), energy of elastic deformation (α); Abscissa - mineral saturation, 1 - $y = 15.4 \cdot 443.6^x$, $r = 0.960$; 2 - $y = 439.5 \cdot 357.3^x$, $r = 0.970$; 3 - $y = 0.42 \cdot 238^x$, $r = 0.958$.

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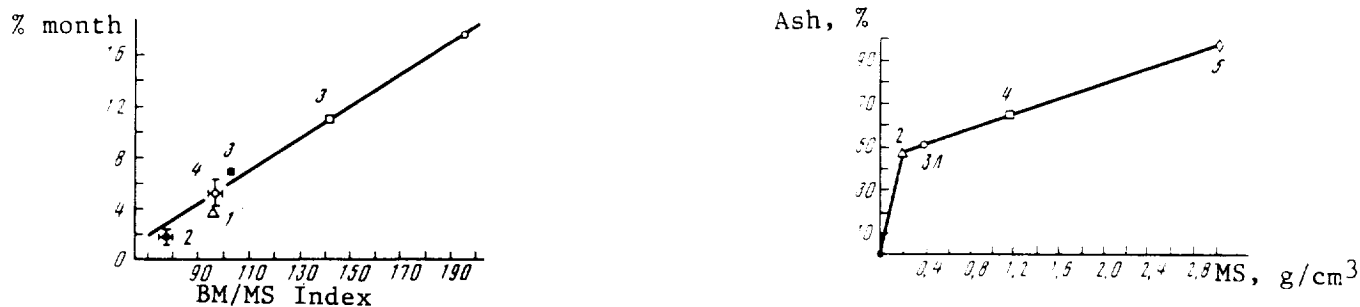


Figure 43: Rate of dystrophy of bone structures (in % month) as a function of the relative index of osteoporosis (basal metabolic rate/mineral saturation)

1 - humans (Schneider, 1977); 2 - humans (weightlessness); 3 - dogs; 4 - rats; light and dark circles indicate error limits of mean values - for hypodynamia, and weightlessness, respectively

Figure 44: Relationship between mineral saturation and ash content:

1 - demineralized collagen; 2 - humans, bone tissue of vertebrae; 3 - dogs, bone tissue of the proximal epiphysis of the femur. 5 - hydroxyapatite. Abscissa: mineral saturation, g/cm³; Ordinate - ash content, %

PAPERS:

P1205(27/90)* Karkishchenko NN.

Specification for an "ideal" drug to prevent space motion sickness (space adaptation syndrome).

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 33-36; 1989.

[16 references; 3 in English]

Neurophysiology, Space Adaptation Syndrome; Human Performance, Mental Work Capacity
Humans, Patients, Vestibular Tolerance, Diminished
Rotation, Pharmacological Countermeasures

Abstract: The goal of this work was to identify the effects and mechanisms underlying the action of drugs holding promise for use in prevention of space motion sickness.

A total of 179 subjects, aged 19-26, with diminished vestibular tolerance participated in the experiment. Motion sickness was induced through a rotation and vestibular stimulation. Rotation was continued until the subjects developed symptoms of level II-III in severity. The signal to terminate vestibular stimulation was the onset of nausea or vomiting. Subjects were assigned to drug conditions (single or multiple doses taken internally) by a double blind method including a placebo condition, with scopolamine in a dose of 1 mg used as a standard. The antimotion sickness efficacy of the drugs was assessed by recording length of time a subject tolerated exposure to acceleration, the dynamics of development of clinical symptoms of motion sickness, and changes in pulse rate during motion sickness induction and spectral characteristics of EEG. Cognitive performance was studied through a computerized test. The results were processed and tested using the Wilcoxon paired measurements test. Drugs used and their efficacy are described in the table.

A single dose of diphenin (dilantin, phenytoin) or dapkene (valproic acid) [both anticonvulsants], and repeated daily doses of potassium orotate and pyracetame (described elsewhere as a cyclic analogue of GABA) were associated with significantly longer tolerance of complex acceleration compared to scopolamine. The anti-motion sickness effects of these drugs also included faster reduction of symptoms of vestibuloautonomic disturbance, smaller changes in pulse rate and in the amplitude of spectral EEG characteristics compared to motion sickness induction (in which no drugs were used).

The mechanisms underlying the protective effect of potassium orotate may involve not only activation of nucleic acid synthesis, but also accumulation of GABA in brain tissue accompanied by decreased glutamate. The interaction of antiepileptics and neuroactive amino acids may also play an important role, since diphenin and depakene have an activating effect on GABAnergic systems, and a depressing effect on glutamate and aspartatergic systems. In addition, depakene inhibits glycine metabolism, and the effects of glycine and excitatory amino acids affect release of acetylcholine. The therapeutic effects of diphenin and depakene may also be related to their tendency to depress the hypothalamic beta-endorphin system through mediation by GABAnergic neurons. At the same time, GABA, glutamate, glycines, endogenous agonists of opiate receptors, and acetylcholine participate at the level of the vestibular nuclei in the processing of information about movement of the body in space. Their effects on the opiate, dopamine- and histaminergic mechanisms may be significant for the suppression of the emetic reflex. An "ideal" pharmacological agent for preventing space motion sickness should have two properties in addition to inhibition of vestibular reflexes. It should increase antiorthostatic tolerance and improve mental and physical performance.

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Used in combination, the most effective drugs exert a powerful corrective effect on mental performance, as assessed by performance on the "missing number test."

The effects and mechanisms of action of the ideal antimotion sickness drug, derived from the current results and data in the literature, are presented in the figure.

Table The effects of drugs on endurance time for complex acceleration

Drug	Endurance time, seconds M±m		
	1	2	3
Placebo	118.3±10.7	123.3±11.3	104.2±9.6
Scopolamine	136.1±9.2	167.8±10.0**	123.3±7.3
Diphenin, 200 mg	123.2±11.9	187.8±22.3*	146.3±17.4
Diphenin, 300 mg	104.4±16.0	170.0±28.3**	162.8±27.1
Placebo	144.1±7.8	153.2±7.6	106.5±5.3
Scopolamine	139.3±8.2	162.7±11.4*	116.8±8.2
Depakene, 300 mg	99.1±9.6	131.7±18.7	132.9±18.7
Depakene, 450 mg	99.3±12.0	166.4±17.3*	167.6±17.5
Placebo	112.5±8.2	115.0±9.4	102.2±8.4
Scopolamine	120.5±11.5	144.5±12.6*	119.8±10.5
Pantogam, 1000 mg	118.8±13.2	133.1±26.9	112.1±22.6
Pantogam, 1500 mg	116.9±9.9	141.9±18.5	121.4±15.9
Placebo	143.8±17.6	171.3±13.6	119.2±9.4
Scopolamine	135.6±6.7	149.4±22.4	110.2±16.5
Potassium orotate,			
5-7 days	130.0±18.8	131.3±13.2	101.0±10.1
12-14 days	97.5±15.8	239.5±44.5**	245.6±45.6
Placebo	125.9±17.8	138.4±16.5	109.9±13.1
Scopolamine	128.5±15.9	161.8±22.7**	125.9±17.6
Pyracetame, 2000 mg			
one dose	120.0±22.0	230.0±57.7	191.7±48.1
3 days	105.0±12.4	212.5±40.4*	202.4±38.5
7 days	127.9±16.4	280.8±46.1**	219.5±36.0
14 days	104.5±13.3	144.5±26.1**	138.3±5.0

1 - endurance time before drug (seconds)

2 - endurance time after drug (seconds)

3 - 2 as a percentage of 1

Repeated doses: three doses per day - potassium orotate in a daily dose of 40 mg per 1 kg body weight; pyracetame in a daily dose of 30 mg per 1 kg body weight.

* - $p < 0.05$; ** $p < 0.01$

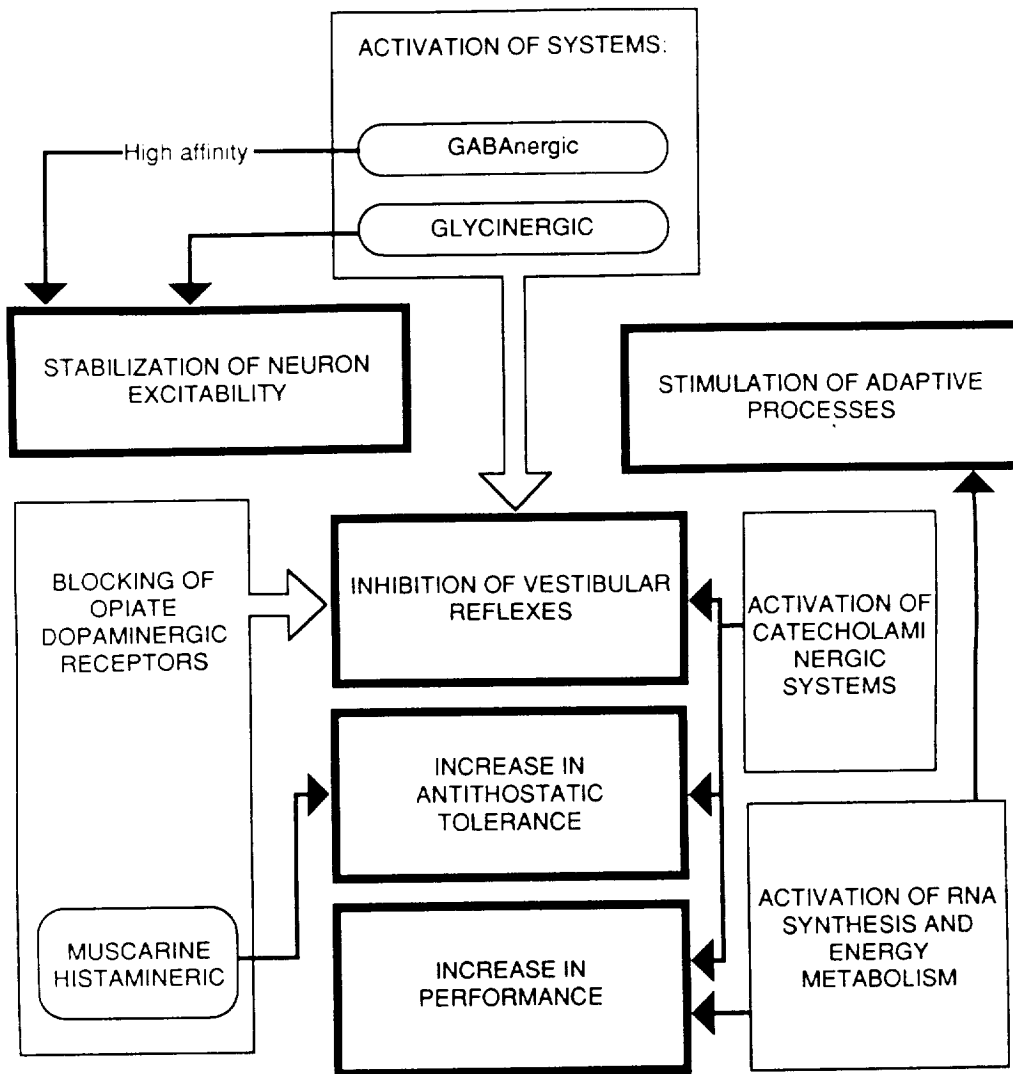


Figure: Effects and mechanisms of the "ideal" pharmacological agent for prevention of space motion sickness

P1214(27/90)* Verbitskaya LB, Fedorenko VS, Kabitsyna RA..

Remote ultrastructural changes in cerebellar cortex of rats after exposure to accelerated carbon ions.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 71-77; 1989.

[2 references; 1 in English]

Neurophysiology, Cerebral Cortex

Rats

Radiobiology, Accelerated Carbon Ions, γ -Radiation; Remote Effects

Abstract: Experiments were performed on sexually mature male Wistar rats. One group was irradiated with carbon ions with a flux rate of 10^4 particles/cm². Animals in a second group were irradiated with γ -radiation using ⁶⁰Co in a dose of 1.0 Gy, and 1 day later with the above dose of carbon ions. Group 3 were irradiated only with γ -radiation, while group 4 was an unirradiated control. The rats were irradiated with carbon in a synchrophasotron. Following a 1-, 3- or 6-month period after irradiation, the animals were sacrificed and the brain tissue processed for electron microscopic study. Semi- and ultrathin sections were prepared and studied using light and electron microscopes.

Irradiation led to dystrophic damage to neurons and glial cells. However, destructive changes were severe in the groups exposed to carbon ions. Indeed, carbon ions with flux of 10^4 particles/cm² (LET = 1 kequiv/ μ m) were more effective than γ -radiation in a dose of 1.0 Gy. Exposure to γ -irradiation followed by carbon ion irradiation did not lead to further worsening of pathological processes. Structural damage to the various types of nerve and glial cells differed in nature. Changes in the Purkinje cells were of the "dark" type, while adjacent Bergman glial cells showed changes of the "light" type with edema, and swelling of the cell bodies, their nuclei and outgrowths in the granular layer. In contrast, nerve granule cells showed "light" changes, while adjacent glial cells -- the oligodendrites -- showed thickening of karyo- and cytoplasm, and heightened osmiophilia. It is suggested that these changes in neurocytes and glial elements serve to maintain impaired functions of the neurons, including cell interactions. Study of changes over time in the cerebella of irradiated animals demonstrated that destructive changes progress during the remote period after irradiation. The study is interpreted as demonstrating the possibility of remote damage to cells of the central nervous system, after exposure to even small fluxes of heavy ions.

Figure 1: Purkinje cells and the internal granular layer of the cerebellar cortex of control animals and rats 1 month after irradiation with accelerated carbon ions

Figure 2: Ultrastructural changes in granule cells and synaptic glomerules of the internal granular layer of the cerebellar cortex of rats 1 month after irradiation with accelerated carbon ions

Figure 3: Formation of pathological inclusions, the development of "fissures" in the cytoplasm of Purkinje cells of the cerebellar cortex of rats

Figure 4: Ultrastructure undergoing "dark" type alteration of Purkinje cells and vacuolization of the dendrites of Purkinje cells in the molecular layer

P1227(27/90) Moskalenko YuYe, Beketov AI, Maksimiuk VF, Skoromnyy NA.

Cerebrovascular effects of motion sickness.

Fiziologicheskiy Zhurnal SSSR im I.M.Sechenova.

75(11): 1560-1567; 1989.

[12 references; 2 in English]

Authors' Affiliations: Institute of Evolutionary Physiology and Biochemistry, Leningrad;

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Neurophysiology, Cerebrovascular Effects; Cardiovascular and Respiratory Systems, Cerebral Circulation

Rabbits

Motion Sickness, Head-Down Tilt

Abstract: Past results have suggested that cerebrovascular reactivity data provide indirect information on the compensatory capabilities of the mechanism regulating circulation in the brain. Cerebrovascular activity was assessed from active responses of the cerebral vasculature to provocative loadings, and was expressed as the ratio of a series of cerebral circulatory parameters before and during exposure to the provocative stimulus, motion sickness induction. The effects of motion sickness on the compensatory capacities of the cerebral circulation system were studied in a long-term experiment on rabbits with implanted electrodes in various areas of the frontal and occipital lobes. Experiments were performed on alert animals loosely restrained so as not to cause discomfort. Three types of provocative tests were selected for use in assessment of cerebrovascular activity. The first involved a 1.5-minute period of inhalation of gas containing 10% CO₂ in air, in which reactivity was measured by comparing levels of local cerebral blood flow before and after inhalation using the method of hydrogen clearance from implanted electrodes. The second method involved graded compression of the abdominal cavity for a period of 30 seconds. Vascular response in this case was evaluated using impedance plethysmography recorded from the same electrodes. Reactivity was assessed from dynamics of pulse wave amplitudes on a cerebral plethysmogram. The third test utilized light stimulation. In this case clearance was used to measure intensity of local cerebral blood flow, while impedance plethysmography served to indirectly determine vascular response. Motion sickness was induced using a swing with an arm of 1.3 m and a frequency of 50-55 swings per minute. In another condition motion sickness induction was combined with head-down tilt (-30°). Rabbits exposed to motion sickness induction (swinging) and head-down tilt alone or in combination were examined before and during the provocative stimulation described above. Parameters measured were local cerebral blood flow in the areas of the electrodes and the state of fluid balance in the same areas of brain tissue. The first parameter was measured using hydrogen clearance and the second estimated from results of impedance plethysmography.

Results confirmed that 2 hours of swinging leads to some increase (10-25%) in local cerebral blood flow. As a rule, the reactivity of brain vasculature decreased to all three provocative tests after swinging. An exception was retention of vascular reactivity in the visual cortex in response to light stimulation. These results, combined with the general tendency for local brain blood flow to increase, suggested a hypothesis that the motion sickness induction procedure decreased the adaptive activity of central mechanisms for regulating cerebral blood flow, but left local regulation intact. If these changes are neurogenic (activation of cholinergic systems has been demonstrated in motion sickness), it is likely that there would also be a change in the fluid balance of brain tissues, impeding outflow of blood from the skull. If motion sickness is accompanied by factors leading to impeded outflow from the skull, then the compensatory effects will be disrupted. The latter will lead to hydration of brain tissue and increase in intracranial pressure.

NEUROPHYSIOLOGY

Effects of head-down tilt are typically well compensated, but at the cost of some strain on regulatory mechanisms. If motion sickness does diminish the adaptive capacity of the cerebral circulation system, if combined with head-down tilt uncompensated effects are likely to be found, including hydration of brain tissue. To test this hypotheses, rabbits were exposed to a combination of head-down tilt and swinging, and information on brain tissue hydration obtained indirectly from impedance plethysmograms. Results showed significant impedance plethysmographic changes consistent with increased hydration in response to the combination of head-down tilt and swinging, greater than changes occurring after head-down tilt alone, and most marked in the visual cortex. Normalization occurred only 1.5-2.0 hours after treatment terminated.

The authors conclude that their results show that the effect of motion sickness induction on the complicated system of regulatory processes responsible for maintaining adequate blood supply to brain tissue under changing environmental conditions may be considered the major cerebrovascular effect of this factor. When motion sickness is induced, in all likelihood, coordination among the individual components of the mechanisms regulating cerebral circulation is disrupted and there is a tendency for central regulatory effects to be depressed, while local ones are retained. General changes in level of local cerebral blood flow that can be observed in motion sickness, most likely reflect the lack of coordination among individual components of the mechanism regulating cerebral circulation. An important consequence of these changes occurring in response to motion sickness is a tendency for physical homeostasis of neural tissue to be disrupted, increasing the risk of brain edema.

Figure 1: Changes in reactivity of the vasculature of the sensorimotor and visual areas of the cerebral cortex in response to light stimulation and abdominal compression as estimated from the ratio of pulse waves in a local impedance plethysmogram at rest and during the provocative test

Figure 2: Change in cerebral blood flow in inhalation of carbogenic gas in the sensorimotor area of the brain

Figure 3: Change in components of impedance - extracellular, intracellular, and capacitance -- in the sensorimotor and visual areas of the brain in response to head-down tilt, motion sickness induction and their combination

Figure 4: Pulse waves of a local impedance plethysmogram in the sensorimotor and visual cortices at rest in head-down tilt, motion sickness and their combination 30 and 60 minutes after onset of exposure

PAPER:

P1228(27/90) Anishchenko TG, Burshina SN, Shorina LN.

An analysis of factors determining sex differences in the stress responses of white rats.

Byulleten' Eksperimental'noy Biologii i Meditsiny.

1989(11):616-618.

[15 references; 3 in English]

Authors' affiliation: N.G. Chernyshevskiy University, Saratov

Psychology, Stress Response

Rats, Males and Females

Gender Differences, Genetics

Abstract: This work studied stress responses of infantile, normal adult, and castrated male and female white rats, and female rats androgenized in infancy, as a means to determine the factors responsible for sex differences in these responses. "Emotional-pain stress" was created by immobilizing animals for 10 minutes; "emotional" stress was created in animals paired with the immobilized ones by the sight and cries of their "partners." Intensity of the stress response was assessed by changes in concentrations of corticosterone in the adrenal gland and blood plasma measured fluorometrically. Stress responses were studied in sexually immature rats, adult untreated rats, rats castrated 3 weeks before the experiment and adult females that had been injected at the age of 1 day with 1 mg testosterone propionate. A total of 362 animals were used.

In adult rats, sex differences in stress responses were marked. In the emotional (observational) stress situation level of corticosterone increased by a factor of 2 in females and 1.4 in males. In the emotional situation the females displayed heightened motor activity, showing clear "resonance" with the other animal. The males displayed a passive defense reaction of the "freeze" type. In the emotional-pain stress (actual immobilization) situation, plasma corticosterone increased by a factor of 4 in females and 2.3 in males. Castrated animals retained the sex differences in response to stress. In the females in the emotional stress paradigm, corticosterone increased in the adrenal gland and plasma by factors of 2 and 2.5, respectively. In the males the corresponding factors were 1.4 and 1.6. In the pain-stress paradigm, castration led to decreased increases in secretion of hormones for both sexes, but sex differences were retained. In sexually immature animals corticosterone increased in females in the emotional stress paradigm by a factor of 1.5 and 1.4, but in males did not increase in either the adrenal glands or the plasma. In the pain-stress paradigm, synthesis and secretion of the hormone increased by a factor of 1.7 and 2.3 in the immature females while only secretion increased (by a factor of 2.3) in the males, with adrenal concentration not changing. Thus, in immature animals the adaptive capacity as indexed by intensity of the stress response is diminished. However, females display appropriate responses to adverse conditions, while infantile males do so to a much lower extent. These results suggest the ontogenic nature of sex differences. Female rats androgenized as neonates leading to masculinization of the brain still displayed a female type of stress response. The authors conclude that sex differences in stress response are genetically determined and not due to sex hormones or sexual differentiation of the brain.

Figure 1: Reactions of intact rats to emotional stress and emotional-pain stress

Figure 2: Reactions of castrated rats to emotional stress and emotional pain stress

Figure 3: Reactions of sexually immature rats to emotional stress and pain stress

PAPERS:

P1221(27/90) Zukhbaya TM.

Periodicity of hemopoiesis during continuous γ -irradiation with low dose rates.

In: I Vsesoyuznyy Radiologicheskiy S"yezd: Tezisy Dokladov; I Всесоюзный Радиологический Съезд: Тезисы Докладов ю [I All-Union Radiobiological Congress: Paper Abstracts] Moscow, 21-27 August 1989.

Pushchino: USSR Academy of Sciences; 1989.

Author's Affiliation: Institute for Biomedical Problems, Moscow

Hematology, Hemopoiesis, Periodicity

Rats

Radiobiology, γ -Irradiation, Continuous

Translation of abstract: It is well known that after acute radiation in sublethal doses, recovery of the hemopoietic system occurs in phases. Similar fluctuations have been observed in the erythroid population in blood letting, hypoxia and various stress situations. We found that an analogous pattern of change over time occurs in the major hemopoietic bone marrow cells and the lymphoid organs during continuous irradiation of rats.

Thus, during a 3-month period of γ -irradiation (22 hours per day) with a dose rate of 0.4 Gy/day (total cumulative exposure approximately 40 Gy), four periods of sequential changes in the size of populations of different hemopoietic cells were observed. In each period the minimal values of quantities of erythroid and granulopoietic elements in bone marrow were half that of the norm, while maximal values of these same parameters approached baseline. When dose rate was increased to 1.0-2.0 Gy/day fluctuations were damped, while at a greater dose rate of 4.0 Gy/day they disappeared entirely.

The first period in the fluctuating process was analogous to that described in radiobiology as "an abortive increase" and observed in all populations of bone marrow cells (except for the lymphoid), and also the thymus and the spleen. Each cell line differed with respect to intrinsic duration of period and amplitude of fluctuations, which changed as a function of radiation exposure schedule.

The second wave of hemopoietic recovery started on day 10-15 of continuous radiation and covered all hemopoietic cells (including the lymphoid elements of bone marrow) at dose rate of 0.4 Gy/day, attesting to the participation of pluripotent stem cells. At the same time, when dose rate was 1.0 G/day, repeated regenerative surges were observed only in the erythroid and neutrophiloid series, which evidently, are associated with the predominant differentiation of stem hemopoietic cells in this direction to support hemostasis of the most vital elements in peripheral blood.

The phasic nature of changes in the hemopoietic system during continuous exposure to radiation attests to the rhythmic activity of the hemopoietic precursors of the stem and semi-stem type. Prediction of the duration of the period and amplitude of fluctuation of a regenerative wave in exposure to various schedules of continuous radiation may be important in radiation clinics.

CONFERENCE REVIEW:

CR13(27/90)* Gyurdzhian AA, Zorile VI.

The work of the section on Aviation and Space Medicine of the Moscow Physiological Society.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(6): 91-92; 1989.

KEY WORDS: Space Medicine; Aviation Medicine

The section on aviation and space medicine of the Moscow Physiological Society unites approximately 300 specialists (physicians, psychologists, engineers, biologists, and others) interested in the problems of aviation and space medicine. Participants include representatives of civil and military aviation, the aviation industry, institutes of higher learning, and scientific and clinical institutions (Institute of Biomedical Problems of the USSR Ministry of Health, The Central Scientific Research Aviation Hospital, the Yu.A. Gagarin Center for Cosmonaut Training, the central and clinical hospitals and polyclinics of the Ministry of Civil Aviation, The Civil Aviation Scientific Research Institute, the Department of Aviation Medicine of the Central Medical School, etc.).

The work of the section is directed by a bureau, chaired by N.M. Rudniy, with V.I. Zorile as scientific secretary. Sessions are generally held once a month in the quarters of the Department of Aviation Medicine of the Central Medical School (7 Peschanaya Street, Moscow). Joint sessions are also held with other sections of the Moscow Physiological Society, for example, the section on occupational physiology.

In 1988 there were 10 meetings in which more than 30 papers were delivered and discussed. Two sessions were devoted to the International Day of Aviation and Cosmonautics and were conducted at the regular session of the 18th Gagarin Lectures.

Among the papers discussed were "New Methods for Evaluating Performance of a Flight Crew" (Ye.A. Yevseyev, S.L. Shapovalov, T.I. Milyavskaya); "Electroencephalographic Correlates of Pilot Job Performance" (D.I. Shnachenko); "Lipid Metabolism in Flight Personnel and Methods for Identifying Hyperlipidemia" (S.A. Bugrov, R.K. Kiselev, T.A. Orlova); and other works of significant scientific and practical importance for medical support of flight personnel.

In 1988 members of the section produced more than 10 monographs, 15 texts, and manuals for flight surgeons, flight crews, and cosmonauts. Among these were: "Reserves of the Human Psyche" (L.P. Grimak, published in a mass edition by Politizdat); "Biological Effects of Lunar Soil," (V.V. Kustov, V.I. Belkin, G.G. Kruglikov, Leningrad, Nauka, 1988); and "A Handbook on Functional Rehabilitation of the Vision of Flight Personnel in Civil Aircraft," (V.F. Tokarev, S.L. Shapovalov, T.I. Milyavskaya, Y.A. Yevseyev, Moscow, Vozdushniy Transport, 1988).

The meeting of the section on 26 October 1988 was devoted to analysis of the articles in the journal "Space Biology and Aerospace Medicine" for 1987. Professor N.M. Rudniy presented a report on the topic. Eight participants took part in a discussion.

They noted that the journal is of great practical and theoretical assistance to specialists in aerospace medicine and interdisciplinary areas. The unanimous opinion of those who spoke was that the journal generally meets the needs of its readers.

However, along with the general positive evaluation of the journal, important criticisms and suggestions focused on further improving the efficiency of the editorial board and the scientific and practical significance of the articles published. In particular, opinions were expressed

that the articles in the journal are predominantly theoretical, narrowly specialized works on space biology, with few articles on aviation medicine (N.A. Razsolov). It was also stated that little attention is paid to the psychophysiology of flight tasks, selection and training of pilots and cosmonauts, improvement of the system of medical monitoring, and increasing flight safety (V.I. Zorile, K. A. Pimenova). Publication of articles on these issues would attract the attention of many specialists in aviation and would thus increase the number of readers, subscribers and authors who are flight surgeons and/or scientists working in related areas. This is not the first time complaints were heard concerning the length of time it takes for a manuscript to be published on the pages of the journal. Increase in efficiency in the publication of articles, among other measures, would help to turn the journal into a monthly publication, (instead of bimonthly).

P.V. Vasil'yev, a member of the journal's editorial board, noted in his talk that few articles dealing with aviation are submitted, although the editors try to give them preference in publication.

A major part in increasing reader participation must be played by the section on aviation and space medicine of the Moscow Physiological Society, which can serve as a vehicle for operational scientific communication among specialists in aviation and space medicine. The editors can make broad use of the section meetings to obtain reader feedback. A number of special measures can be undertaken to achieve this. For example, a section could recommend that material that has been presented and discussed be published as articles or abstracts in the journal. The editorial board of the journal could suggest particularly critical and complex issues in aviation medicine for discussion at section meetings. It would be desirable if reports on past and planned section meetings were published in the pages of the journal.

The election of members of our section to Academies -- Professor A.I. Grigor'yev as a corresponding member of the USSR Academy of Medicine as a specialist in "Space Biology and Medicine"; and Professor V.A. Ponomarenko as a corresponding member of the Academy of Pedagogical Sciences as a specialist in "Occupational Training" and member of the presidium of that organization -- are acknowledgements by the scientific community of the role of aerospace medicine in the development of Soviet science. A representative of space pharmacology, V.S. Shashkov has been elected corresponding member of the USSR Academy of Medicine as a specialist in "Pharmacology."

Membership of the section on aviation and space medicine have elected a representative to the of USSR Congress of Peoples Deputies. At the Scientific Conference of Scientific Societies and Associations at the USSR Academy of Sciences, held 22 and 23 March 1989 in the Moscow House of Scientists, N.P. Bekhterev, academician and director of the Scientific and Research Institute of Experimental Medicine of the USSR Academy of Medicine, and member of the presidium of the I.P. Pavlov All-Union Physiological Society, and O.G. Gazenko, consultant to the director of the Institute of Biomedical Problems of the USSR Ministry of Health, and president of the I.P. Pavlov All-Union Physiological Society, were elected as people's deputies.

N.A. Razsolov, K.A. Pimenova, S.L. Shapovalov, Ye.Ye. Nikolayevskij, I.N. Chernyakov, V.V. Chuntul, and A.A. Shishkov participated actively in the work of the section in 1988.

In 1988, 12 scientists, graduate students, adjuncts, flight surgeons, and clinical specialists were accepted as members of our section of the Moscow Physiological Society. In 1989, plans call for holding nine meetings of the section on aviation and space medicine. Topics to be covered include diagnosis of functional state of the cardiovascular system and visual systems of humans during flight, and prevention of fatigue and improvement of techniques for restoring performance levels of crews after long flights. In addition, a symposium is planned on the topic of "psychophysiological aspects of increasing the safety of flights on modern flight vehicles"

with participation by specialists in various institutes. One meeting will be devoted to the scientific work of medical doctor, professor and winner of the USSR State Prize, P.K. Isakov, in honor of his 80th birthday.

Finally, certain initiatives and accomplishments of the I.P. Pavlov All-Union Physiological Society should be noted. The publication of a new informational series, "Physiology. Informational material of the I.P. Pavlov All-Union Physiological Society," edited by the president of the society, academician O.G. Gzenko is an outstanding accomplishment. These publications provide timely information concerning the work and decisions of the Division of Physiology of the USSR Academy of Sciences, the Presidium and Central Soviet, and the republic societies concerning congresses, conferences, symposia, seminars, meetings, and schools in physiology, and also bibliographic information about books to be published in physiology, medicine, biology and mixed disciplines.

The international ties of the All-Union Physiological Society have increased significantly. In 1988 for the first time for a society of the USSR Academy of Sciences, an agreement was signed to enable scientific collaboration between the physiological societies of the USSR and USA, in which physiologists from Czechoslovakia, Bulgaria, Finland, and the People's Republic of China will also participate.

Special Feature: Essay by N. Gurovskiy; **In the Interests of Public Health**
In: *Aviatsiya i Kosmonavtika*; 11/89

KEY WORDS: Space Medicine, Operational Medicine, Public Health, Equipment and Instrumentation, Personnel Selection, Hematology, Biological Rhythms

Today there is not a single area of human activity that has failed to feel the stimulating effects of cosmonautics. This field has enriched not only our knowledge of space and the Earth, but also public health. As manned space flight has developed, techniques for monitoring the health status of cosmonauts have improved, along with understanding of human potential and what is required in order to prepare humans to undergo the rigorous ordeal of space flight. Now space medicine is providing health benefits to people on Earth too.

Here are some concrete examples of the interrelationship of space and terrestrial medicine.

In its early days, space medicine had to solve the problems involved in selecting and training cosmonauts for flight, developing specifications for the environment in weightlessness and the associated life support systems, and assessing physiological responses to space flight factors. Scientists beginning work in this area were brought up against the inadequacy of our knowledge concerning the responses of a healthy individual in various situations and the optimal concentrations of harmful contaminants in the spacecraft atmosphere. The need to answer such questions led to special research to determine the boundaries between pathology and the norm. The results of these studies began to be used by clinicians in treating their patients.

In examining potential cosmonauts, existing methods of pilot selection were made more precise, while new methods were developed to reveal latent pathology. Now these methods have been adopted in clinical practice, for example, in the study of the vestibular system and identification of latent coronary insufficiency.

As is well known, weightlessness induces deconditioning of the muscle system, changes in cardiovascular functioning, bone tissue, and mineral metabolism. To improve understanding of these phenomena, research was undertaken to study the physiological effects of restricting motor activity. The bedrest paradigm is currently used as a laboratory model of weightlessness.

It would seem natural to question the possible relevance of these studies for public health. It has turned out that they are of direct relevance. Hypokinesia is an extremely significant etiological factor in the development of diseases, especially of the cardiovascular system.

Research on healthy human subjects revealed a number of symptoms characteristic of the state of hypokinesia. It is essential that clinicians be aware of these symptoms when, while treating a patient, they must differentiate between the symptoms attributable to the primary disease and those due merely to limited motor activity.

The use in space medicine of constant remote monitoring has found practical application in clinics, health resorts, and athletics. In addition, special equipment has been developed to embody the principles utilized in space medicine. Such systems are used in the postoperative and resuscitation (intensive care) units of many hospitals. The "Telekont" biotelemetric system, designed for monitoring the condition of patients who have suffered myocardial infarction, is currently being tested.

It would be reasonable to use satellite communication lines for hospitals remote from the leading medical centers of the country. There is currently nothing that in principle prohibits implementation of such "remote diagnosis." The prototype of such a system was validated during the work of the 28th Soviet expedition to the Antarctic. Using portable medical instruments, a

physician in the tent recorded an electrocardiogram and measured the blood pressure of one participant in the expedition. These data, in the form of a digital radiogram, were transmitted by satellite to Moscow where they were decoded and analyzed and the conclusions drawn sent back via satellite to the physician in the Antarctic.

The principles of "remote diagnosis" formed the basis for the operation of a mobile automated laboratory ("Avtosan") for mass examination of the population. This laboratory was equipped with virtually the same medical apparatus as the Salyut space station.

Examination of a single patient, involving measurement or derivation of approximately 15 parameters, requires about 15 minutes. Two portable computers perform analysis of the data, automatically take the patient's history, and process all information. All the information generated by an examination may be entered into the data base and used for future annual examinations.

Unfortunately, at present the number of "space methods" available is far from sufficient to cover the entire population.

The "Oxymeter" device developed to study oxygen supply to cosmonauts is now used clinically for diagnosis of a number of diseases: in dentistry for periodontosis, for plastic surgery, and for ischemic heart disease.

Specialists in space medicine have developed a methodology for studying intestinal microflora that is used in clinical practice for studying the condition of patients with chronic diseases of the gastrointestinal tract.

A method of detoxifying donated blood for long-term storage involves passing blood that has undergone preliminary incubation with adenine and inosine, through a column with a sorbent (type SKN-100). Blood treated this way may be stored for up to 52 days. In clinical practice, donated blood preserved with a glucose-citron preservative can be kept for 10-15 days. The difference is significant. The Committee on Discoveries and Inventions has evaluated the proposed method, concluding that it has great economic significance, providing enormous savings in the cost of blood storage.

In space there is no natural alternation of day and night and the synchronizers for many physiological functions are no longer present. The study of biological rhythms is critical for passenger aircraft flight across time zones and the numerous jobs involving shift work. Work on chronobiology performed in the context of space biology and medicine has made an important contribution to this problem.

In conclusion, I would emphasize one more issue. In selection of cosmonauts, psychological examination helps us identify latent and atypical disturbances, predict behavioral and emotional responses of an individual to stress, define a number of principles relevant to human interactions within a group, and find rationales for principles of group selection. This has allowed us to successfully select the members of a group for joint performance, particularly in team formation in sports, selection of groups for expeditions to the North Pole or to climb mountains.

Thus, space medicine, besides stimulating the development of general biology and the practice of public health, has enriched these areas with new methods and ideas.

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